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CHANGES IN BRAIN VOLUME DURING ANESTHESIA: THE EFFECTS OF ANOXIA AND HYPERCAPNIA

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This investigation was instigated by an unfortunate anesthetic complication which occurred in the Neurosurgical Service of the Massachusetts General Hospital in 1938. A young woman who was rapidly losing her vision because of a hypophysial adenoma that compressed the optic chiasm had a complicating severe bronchiectasis. Operation was therefore undertaken with only local infiltration anesthesia. The moment the tumor had been satisfactorily exposed, however, the patient lost her nerve and insisted that she be placed under general anesthesia. In view of the extensive bronchiectasis it was decided that a relatively low concentration of nitrous oxide with oxygen might be given. Since an intratracheal tube had not previously been inserted and it was deemed inadvisable to disturb the patient's position sufficiently to insert one, it appeared wiser not to use ether. With the onset of a minor degree of cyanosis as the gas was administered, the exposed cerebral hemisphere began to swell. Elevation and retraction of the frontal lobe at once became impossible, and the cerebral cortex soon herniated so that it protruded through the craniotomy opening. All thought of removing the adenoma had to be given up, and in order to replace the bone flap it was necessary to stop administration of the anesthetic and to permit the patient to breathe room air. As the oxygen saturation of the blood returned to normal, the cerebral swelling and herniation rapidly subsided.

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Similar anesthetic complications with the use of ether were by no means rare before intratracheal intubation for anesthesia eliminated respiratory obstruction and permitted the anesthetist to insure constant adequate oxygenation of the blood and the tissues.

Experiments with animals were undertaken to learn more about the factors which cause swelling of the brain in the course of intracranial operations. The following factors may under various conditions produce enlargement of the brain: engorgement of the vascular tree; escape of fluid from the capillaries into the intercellular spaces (edema); swelling of the nerve and glial cells, and increase in the size of the ventricles. We have not attempted to distinguish between an increase in intercellular and an increase in intracellular fluid and must therefore include these two entities under the term "swelling of the brain." Accurate methods of measuring swelling of the brain in animals have not been described heretofore, nor has any satisfactory method of determining the total volume of blood in the brain been published. Quantitative methods and a number of other procedures which will facilitate the study of changes in brain volume in other conditions have been developed in the last three years in the course of a large series of experiments with animals.

MATERIAL AND METHODS

Cats were used as experimental animals and proved most satisfactory. They were fed a normal diet until the morning of the experiment. Healthy medium-sized adult animals were selected; animals with any evidence of respiratory infection or malnutrition were rejected. Although the plasma protein level was not determined for any of these animals, it is most unlikely that the level was lowered.

Determination of Cerebral Swelling.—Various proposed methods of measuring swelling of the brain have been described and critically reviewed by Alexander and Looney.[1] The most important are: (1) the differential ratio of brain volume to cranial capacity, which was utilized by Rieger,[2] Reichardt[3] and Rudolph[4]; (2) the total water content of the gray and the white matter of the brain, which has been used extensively by Pilcher.[5] In addition to noting the difficulties of separat-

1. Alexander, L., and Looney, J. M.: Physiochemical Properties of Brain, Especially in Senile Dementia and Cerebral Edema, Arch. Neurol. & Psychiat. **40**:877-902 (Nov.) 1938.

2. Rieger, K.: Eine exakte Methode der Kraniographie, Jena, Gustav Fischer, 1885.

3. Reichardt, M.: Ueber die Bestimmung der Schädelkapazität an der Leiche, Allg. Ztschr. f. Psychiat. **62**:787-801, 1905; Zur Entstehung des Hirndrucks bei Hirngeschwülsten und anderen Hirnkrankheiten und über eine bei diesen zu beobachtender besondere Art der Hirnschwellung, Deutsche Ztschr. f. Nervenh. **28**: 306-355, 1905.

4. Rudolph, O.: Untersuchungen über Hirngewicht, Hirnvolumen und Schädelkapazität, Beitr. z. path. Anat. u. z. allg. Path. **58**:48-87, 1914.

5. Pilcher, C.: Experimental Cerebral Trauma: The Fluid Content of the Brain After Trauma to the Head, Arch. Surg. **35**:512-527 (Sept.) 1937.

ing the gray and the white matter in a small animal and of dehydrating representative areas to a constant weight, Alexander pointed out that changes in brain volume cannot be expressed in the simple terms of water content of either the gray or the white matter and that there is no correlation with gross cerebral edema.[6] On the other hand, the differential ratio of brain volume to skull capacity is a simple and straightforward method of measuring cerebral swelling (due to increase either of intercellular or of intracellular fluid) which can be determined with ease and considerable accuracy.

We have modified the method reported by the previous observers for measuring the volume of the brain and the capacity of the skull in the human postmortem specimen to permit accurate determinations in the small head of the cat. The only special piece of apparatus necessary is a volumetric flask of approximately 150 cc. capacity fitted with a wide-mouthed ground glass cover holding a filling tube 1.5 mm. in diameter with an engraved level to mark an exact point of filling and holding also a thermometer (fig. 1). The flask is filled from a buret through a lumbar puncture needle inserted within the filling tube, with sufficient space around the needle to let air escape. The flask must be calibrated for use at the temperature of the laboratory. We made all the determinations cited in this paper on exsanguinated brains.

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6. Pilcher [5] and Alexander and Looney [1] used the method of drying to constant weight but failed to obtain a significant difference between normal brains and brains which would be expected to be edematous. Pilcher interpreted this as an indication that these brains were not edematous, while Alexander and Looney stated that water content is not quantitatively correlated with cerebral edema and that comparison of the brain volume with the capacity of the cranium is needed. Pilcher (Experimental Cerebral Trauma: II. Further Observations on the Fluid Content of the Brain Following Trauma to the Head, Surg., Gynec. & Obst. **72**: 755-757, 1941) has replied that if the water content is not increased, edema is not present and has denied the validity of Alexander's criteria of edema.

We believe that this controversy may be resolved as follows:

The average volume of the brain in the normal animals under pentobarbital sodium anesthesia in table 2 is 27 cc. The corresponding brain volume for the animals with anoxia of table 3, corrected for the difference in the average volume of the skull in the two series, would be 28.4 cc. This represents an increase of 5.2 per cent in the volume of a brain when it becomes edematous. If one assumes that the edema fluid consists entirely of water, the following is true of a 1.0 Gm. sample of gray matter, which contains normally 80 per cent water:

	Weight of Sample (Gm.)	Weight of Edema Fluid Present (Gm.)	Weight of Normal Gray Matter Present (Gm.)	Solids (= 20% of Weight of Normal Gray Matter) Present (Gm.)	Total Water Content (Gm.)
Normal brain....	1.00	0.00	1.00	0.20	0.80
Edematous brain	1.00	0.05	0.95	0.19	0.81

Thus an increase in the brain volume of 5.2 per cent is mirrored by a rise in the water content of the gray matter only from 80 to 81 per cent. When the solids in the edema fluid are added, this difference becomes even smaller. It appears doubtful whether so small a difference in water content could be detected by drying to constant weight.

A convenient instrument for the instantaneous decapitation of cats is a large size, double action tree pruner, illustrated in figure 2. After decapitation with this instrument, the great vessels in the side of the neck are cut across again with a sharp knife and the blood drained from the head by massaging the muscles of the neck under a stream of running water and compressing the eyeballs. The soft tissues of the head are then removed. It is best to open the orbits by

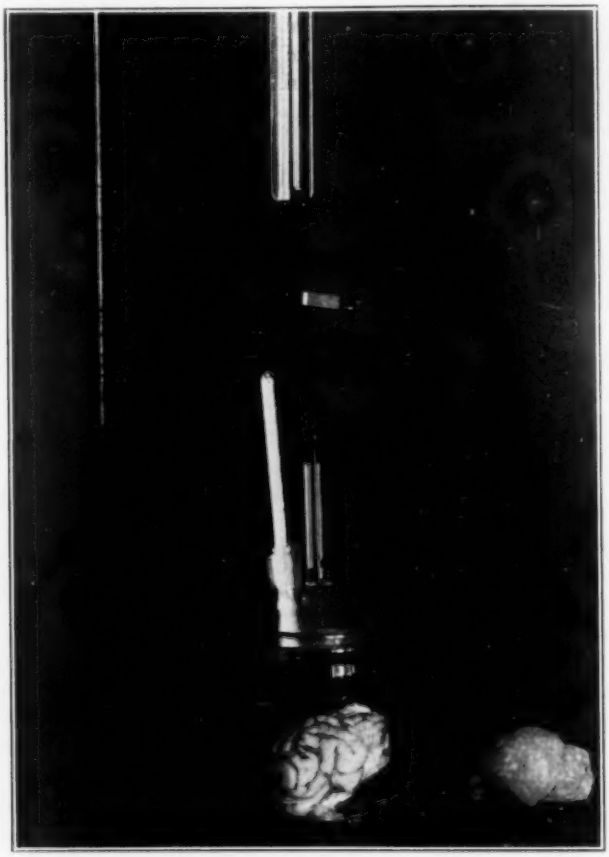

Fig. 1.—Apparatus for measuring brain and intracranial volume. The flask is filled from the buret through the capillary tube in its top by means of a lumbar puncture needle which permits air to escape. The thermometer to the left is for correction of temperature. The paraffin cast of the cranial cavity, to the right of the volumetric flask, appears smaller than the brain because the latter is magnified by the curved wall of the flask.

severing the orbital processes of the frontal and zygomatic bones and to remove the eyeballs. The pharyngeal structures are removed after the mandible has been disarticulated and the muscles separated from the base of the skull. The spinal

cord is cut flush with the foramen magnum before the atlanto-occipital joint has been disarticulated. The skull is then sawed around in the midline sagittal plane and split open like an oyster. With a little practice the brain can be removed with minimal injury to the olfactory lobes and only an occasional nick in the cerebellar hemispheres from the saw. The cranial nerves should be cut close to their respective foramens. It is important that the brain be removed from the skull immediately after death, since it may swell by imbibing cerebrospinal fluid.[7]

If the brain is removed and measured at once, this error is insignificant. The brain is transferred immediately to the volumetric flask, and its volume is determined by measuring the quantity of physiologic solution of sodium chloride which must be added to fill the flask. Cannon,[8] Vandervael[9] and Alexander and Looney[1] have shown that marked swelling occurs when the brain is placed in an isotonic or even in a hypertonic solution. Such imbibed fluid is included in our measurements and thus eliminated as a factor. It is also possible that varying amounts of cerebrospinal fluid in the ventricles may be a source of error. These cavities in the cat are so small that all ventricular fluid is probably expressed in the process of removing the brain from the skull, but the possibility of any error from retained fluid can be obviated by cutting the brain in two by a coronal section across the bodies of the ventricles. Measured in this manner the volume of the average adult cat's brain varies from 25 to 29 cc.

To measure the capacity of the cranial cavity one must reconstruct the skull by fitting the two halves together. This can be done accurately if the width of the skull has been determined before opening by caliper measurements just above the mastoids and at the anterior border of the orbits. It is necessary to use small wooden wedges to compensate for the section removed by the saw and to wire the two halves firmly and accurately together. Prior to reconstructing the skull we remove the dura and the bony tentorium, allowing an arbitrary amount of 0.1 cc. to represent the displacement of the tentorium. The reconstructed skull is then placed nose down in a closely fitting glass jar, and warm liquid paraffin is poured through the foramen magnum to fill the interior of the skull and embed it. Air bubbles which tend to form inside the cranium can be removed by scraping with a heated wire. After the paraffin has hardened (eight hours), it can be chipped away on the outside and trimmed flush with the foramen magnum (as was done previously with the spinal cord). The skull is

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7. An unanesthetized normal animal (59 D) whose head was allowed to remain twenty-four hours and forty minutes at 2 C. before the skull was opened had a differential index of brain volume of 8.5 per cent (normal values, 9.8 to 11.1 per cent). It is suggested that this swelling was due in part at least to imbibition of cerebrospinal fluid by the brain. To check this hypothesis the brain of an unanesthetized animal (61 D) was placed in normal human cerebrospinal fluid at 2 C. for twenty-six hours. The brain increased in volume 0.81 cc., or 3.2 per cent of its original volume. This lowered the calculated differential index of the brain volume from a normal value of 10.1 to 7.9 per cent, a value which indicated definite swelling.

8. Cannon, W. B.: Cerebral Pressure Following Trauma, Am. J. Physiol. **6**:91-121, 1901.

9. Vandervael, F.: Recherches sur l'imbibition du muscle et du cerveau dans les solutions dites physiologiques, Arch. internat. de physiol. **38**:278-292, 1934.

then dissolved away in a bath of concentrated nitric acid, which leaves intact a paraffin cast of the cranial cavity. Excess of wax along the cut made by the saw is scraped away and any bubbles or holes due to wedges are carefully filled with plasticine. The volume of the cast is then measured in the volumetric flask; the determination differs in no way from that of the brain. On the average the intracranial capacity is some 3.0 cc. greater than that of the normal brain.

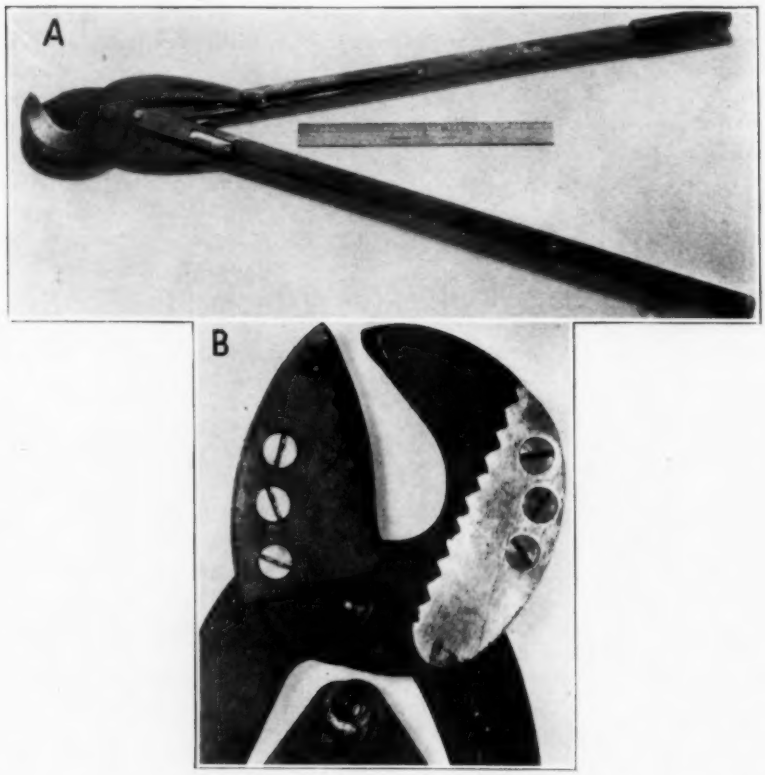

Fig. 2.—*A*, decapitating shears (large size tree pruner) with a foot rule for comparison; for decapitation with exsanguination the cutting blades are applied on the side of the occiput, but in addition the cervical vessels are subsequently severed with a sharp knife to insure free drainage of blood. *B*, the crushing blades; when these are applied beneath the occiput, the cervical tissues are so compressed that no loss of blood can take place.

We have expressed this difference in percentage of the total intracranial capacity; hereafter we shall refer to it as the differential index of brain volume. The exact computation is given from the actual figures for cat 55 D in table 1.

Determination of Blood Volume in Brain Tissue.—The volume of blood in the cerebral tissues has been determined by comparing the color reaction of hemoglobin with purified benzidine against a standard prepared from a sample of the

animal's own blood. This colorimetric hemoglobin method has been adapted by one of us (B. S.) as a modification of the method of Wu,[10] later improved by Bing and Baker.[11] These determinations have been made both on the exsanguinated brains after determination of the brain volume (in this determination the physiologic solution of sodium chloride used to fill the flask is added to the brain) and on unexsanguinated brains. The unexsanguinated brains are prepared by decapitation with the tree pruner (fig. 2) turned so that the crushing teeth clamp off the tissues of the neck en masse. We have not observed back bleeding from the head with this method. The head is then frozen by means of solid carbon dioxide, the skull opened by means of a guillotine and the frozen brain substance removed piecemeal and weighed.

The brain tissue is minced with a knife and ground to a fine paste in a mortar with sand. If the brain volume has been determined, the physiologic solution of sodium chloride used is added, and the total volume in either case is brought

TABLE 1.—*Computation of the Differential Index of Brain Volume from the Figures for Cat 55 D*

$$\frac{\text{Capacity of skull} - \text{volume of brain}}{\text{Capacity of skull}} = \text{differential index of brain volume}$$

Volume of brain	
Volume of flask	168.30 cc.
Physiologic solution of sodium chloride added	142.80 cc.
	25.50 cc.
Capacity of skull (paraffin mold)	
Volume of flask	168.30 cc.
Physiologic solution of sodium chloride added	139.22 cc.
	29.08 cc.
Correction for tentorium	.10 cc.
Capacity of skull	28.98 cc.
Volume of brain	25.50 cc.
Intracranial space not occupied by brain	3.48 cc.
Differential index of brain volume, or percentage of the intracranial space not occupied by brain	12.00 per cent

to 250 cc. with distilled water. A small amount of saponin is added to insure complete hemolysis. The resultant suspension is shaken well and allowed to stand overnight in a refrigerator. To correct variations in the hemoglobin content of the blood of individual animals, a standard solution of blood diluted 1 : 1,000 with distilled water is prepared for each animal from its own blood.

The colorimetric method employed is the benzidine technic of Bing and Baker as modified by Bing.[12] We have found a commercial benzidine reagent (Merck) to be satisfactory for the purpose and have not purified the crude base, as Bing did. The supernatant fluid over the brain suspension is used for the determination. This fluid remains cloudy, but since only 0.1 or 0.2 cc. is used for the determination and the final volume employed for reading is 25 cc., this has caused no

10. Wu, H.: Studies on Hemoglobin: III. An Ultra-Micro-Method for the Determination of Hemoglobin as a Peroxidase, J. Biochem. (Japan) **2**:189-194, 1923.

11. Bing, F. C., and Baker, R. W.: The Determination of Hemoglobin in Minute Amounts of Blood by Wu's Method, J. Biol. Chem. **92**:589-600, 1931.

12. Bing, F. C.: Purification of Benzidine and an Improved Reagent for Estimating Hemoglobin in Blood, J. Biol. Chem. **95**:387-388, 1932.

difficulty in colorimetry. The Duboscq colorimeter has proved most satisfactory for these determinations.[13]

Since we have assumed a uniform distribution of hemoglobin throughout the brain and the supernatant fluid and are unable to verify this assumption, we do not claim absolute accuracy for this method. Checks with blood samples the oxygen capacities of which have been determined by the method of Van Slyke and Neill[14] have been accurate by this method within 12 per cent.

During the experiments a tracheal cannula was always inserted to maintain a wide-open airway, and attention was given to maintaining the dead space at about its normal size. The cannula was cleared of mucus when necessary, but no animals with a tendency to snuffles or other respiratory complications were used.

Rectal temperatures were recorded and not allowed to vary more than a degree by having the animal lie on an electrically heated pad when necessary.

Intracranial pressure was recorded by cisternal puncture, the animal lying on its side and the cistern needle being connected with a capillary manometer. This was filled with physiologic solution of sodium chloride, but precautions were taken to prevent the solution from entering the subarachnoid space, on account of Webster and Freeman's[15] demonstration that the solution may cause a rise in intracranial pressure.

Arterial blood pressure was measured by the direct citrate method of recording with a glass cannula in the femoral artery and a U-shaped mercurial manometer.

Blood for determinations of oxygen and carbon dioxide was drawn under oil from the opposite femoral artery, and oxygen saturations and carbon dioxide content were determined by the methods of Van Slyke and Neill and Shaw and Downing.[16]

Atmospheres of varying oxygen content were made up in a large Douglas bag; oxygen and nitrogen were added in appropriate proportions from a spirometer, and then the final oxygen content of the mixture was measured by the Haldane gas analyzer described by Henderson.[17] During inhalation the tracheal cannula of the animal was connected to the Douglas bag by a series of valves so that the gas breathed entered the trachea directly and was then exhaled into the room (fig. 3). To prevent building-up of carbon dioxide, a minimum of dead space was permitted. When ether anesthesia was induced with varying

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13. The calculation by this method is simple when samples of 0.2 cc. are used.

$$\text{Centimeters of blood in the brain} = \frac{\text{Colorimeter setting on blood sample}}{4 \times \text{colorimeter reading on brain sample}}$$

This result is multiplied by 2 when, with the brains containing larger amounts of blood, only 0.1 cc. of supernatant fluid over the brain suspension is used.

14. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement: I., J. Biol. Chem. **61**:523-573, 1924.

15. Webster, J. E., and Freeman, N. E.: Studies on the Cerebrospinal Fluid Pressure in Unanesthetized Dogs, Ann. Surg. **113**:556-571, 1941.

16. Shaw, J. L., and Downing, V.: The Determination of Oxygen in the Blood in the Presence of Ether by a Modification of the Van Slyke-Neill Technique, J. Biol. Chem. **109**:405-417, 1935.

17. Henderson, Y.: Application of Gas Analysis: IV. The Haldane Gas Analyzer, J. Biol. Chem. **33**:31-38, 1918.

degrees of anoxia, the closed system was further modified to permit addition of ether vapor to the prepared mixture of oxygen and nitrogen (fig. 3).

Depth of anesthesia was followed by observation of the presence or absence of the corneal reflex and of the response of a spinal reflex (contraction of the posterior thigh muscles when the central end of the cut sciatic nerve was stimulated by a faradic current). Every effort was made to keep these animals at a constant level of light surgical anesthesia.

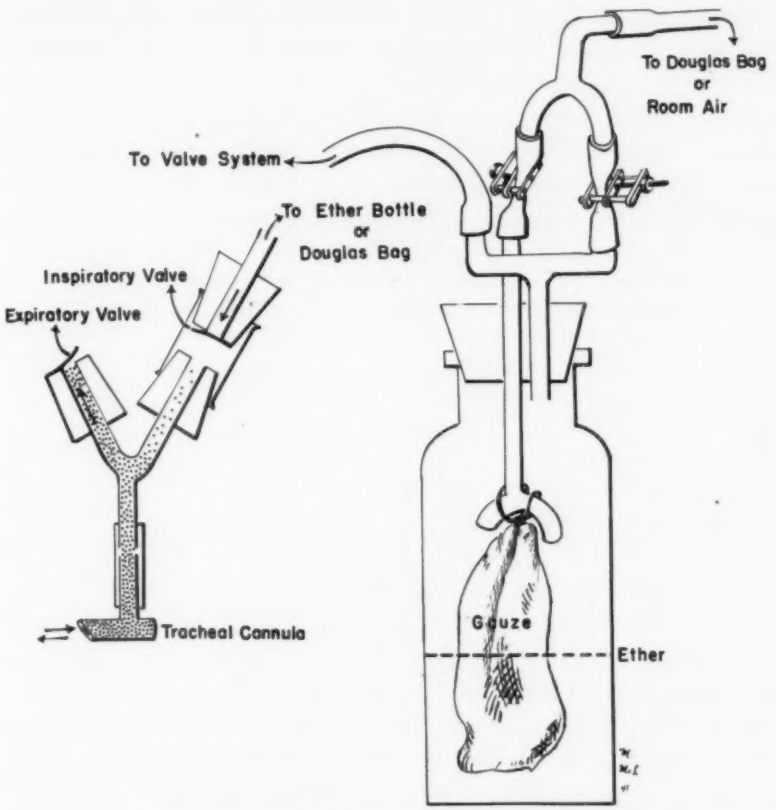

Fig. 3.—The inspiratory and expiratory valves shown in the diagram at the left permit the animal to inhale from the ether bottle or from the Douglas bag and to exhale into the room. The dead space, illustrated by the stippled area, must be reduced to approximately the volume of the upper part of the trachea and the nasal passages. A diagram of the ether bottle is shown on the right. By closing the left pinchcock and keeping the right open, the animal is made to breathe increasing amounts of ether-free atmosphere. The tension of ether vapor is increased by closing the cock on the right.

CONDITIONS WHICH CAUSE SWELLING OF CEREBRAL TISSUE

Differential Index of Brain Volume in the Exsanguinated Normal Cat.—Four normal cats were instantaneously decapitated without anes-

thesia. The proportion of the cranial cavity not filled by brain in these animals is shown in table 2; it averages about 10.5 per cent of the total capacity of the cranium.

In our experiments we were careful to select adult cats. In human beings Rudolph has shown that the percentage of difference between cranial capacity and brain volume increases from 2.5 in infancy to 15 in old age (senile atrophy). In Alexander and Looney's [1] data on pathologic human brains the differential ratio varied from a volume of 29.3 per cent smaller than the cranial capacity in a patient with cerebral atrophy from Pick's disease to the opposite extreme in a patient with epilepsy, whose edematous brain filled the entire cranium. These extreme variations in human postmortem material are probably exaggerated by certain uncontrollable factors such as the duration and degree of capillary anoxia preceding death, the variable drainage of blood from

TABLE 2.—*Differential Index of Brain Volume and Blood Content of Cerebral Tissue of Unanesthetized Normal Cats (Brains Exsanguinated at Decapitation)*

Cat	Differential Index, per Cent	Cat	Blood Content, Cc.
45 D	9.9	112 D	0.21
46 D	11.1	113 D	0.19
47 D	11.1	114 D	0.19
61 D	10.1		
Average	10.5	Average	0.20

the brain after death and the varying length of time before the brain was removed from the cranium.[7]

Differential Ratio of Brain Volume Under Pentobarbital Sodium Anesthesia.—Pentobarbital sodium was injected intraperitoneally into a series of cats in initial doses of 40 mg. per kilogram of body weight, with increments of 5 to 10 mg. per kilogram of body weight as necessary to maintain a constant state of light surgical anesthesia. A tracheal cannula was inserted in every animal to insure an open airway; a warming pad was used to prevent the loss of body heat. Under these circumstances the brain remained approximately the same size as in the unanesthetized cat (up to fourteen hours in cat 51 D). In a series of 5 animals anesthetized with pentobarbital sodium the differential index of brain volume averaged 11.30 per cent (table 3). This differs by 0.80 per cent from the value for the unanesthetized animal (table 2). These figures have been analyzed by the method of Fisher [18] for small series, and the difference was found to be insignificant.

18. Fisher, R. A.: Statistical Methods for Research Workers, ed. 6, London. Oliver & Boyd, 1938, chap. 5.

TABLE 3.—*Data on Cats Under Light Pentobarbital Sodium Anesthesia*

A. Cats Breathing Room Air

Cat	Pentobarbital Sodium, Mg. per Kilogram of Body Weight	Duration of Anesthesia	Oxygen Saturation	Carbon Dioxide Content, Volumes per Cent	Cerebrospinal Fluid Pressure, Mm. of Physiologic Solution of Sodium Chloride	Differential Index of Brain Volume, per Cent	Blood Content, Cc.
48 D	52	3 hr. 15 min.	Color good	....	71	11.7	0.11
49 D	40	5 hr. 6 min.	Color good	....	65	10.0	....
51 D	77.5	13 hr. 55 min.	Color good	....	113	10.1	....
52 D	60	3 hr. 20 min.	89.0 per cent	65.8	55	12.7	0.26
55 D	60	3 hr. 39 min.	92.6 per cent	39.0	62	12.0	0.24
Average						11.30	0.20

B. Cats Breathing 30 per Cent Oxygen and 5 to 10 per Cent Carbon Dioxide

Cat	Pentobarbital Sodium, Mg. per Kg. of Body Weight	Duration of Anesthesia		Carbon Dioxide in Inspired Air, per Cent	Oxygen Saturation, per Cent	Carbon Dioxide Content, Volumes per Cent	Cerebrospinal Fluid Pressure			Differential Index of Brain Volume	Blood Content, Cc.
		Total	Hypercapnia				Onset	Maximum	Final		
81 D	40	3 hr. 15 min.	24 min.	10	90	51.4	98	215	112	10.0	....
115 D	49	2 hr. 7 min.	32 min.	10	98.6	51.0	..	...	...	...	0.20
116 D	47	1 hr. 40 min.	35 min.	5.0	100	29.1	..	...	...	...	0.16
117 D	40	1 hr. 27 min.	43 min.	5.6	100	42.7	..	...	...	...	0.15

TABLE 4.—*Data on Cats Under Light Pentobarbital Sodium Anesthesia*

A. Cats with Anoxia

Cat	Pentobarbital Sodium, Mg. per Kg. of Body Weight	Duration of Anesthesia		Oxygen in Inspired Air, per Cent	Carbon Dioxide in Inspired Air, per Cent	Oxygen Saturation, per Cent	Carbon Dioxide, Volumes per Cent	Cerebrospinal Fluid Pressure			Differential Index of Brain Volume, per Cent	Blood Content, Cc.
		Total	Anoxia					Onset	Maximum	Final		
63 D	50	4 hr. 4 min.	1 hr. 24 min.	9.3	0	79.8	28.2	56	59	59	5.6	0.11
64 D	50	5 hr. 35 min.	29 min.	5.1	0	42.0	17.1	80	116	57	6.3	0.22
65 D	50	4 hr. 58 min.	39 min.	9.3	0	80.6	35.5	83	195	80	7.4	0.34
66 D	50	6 hr. 32 min.	1 hr. 59 min.	9.3	0	70.7	34.8	55	134	134	6.9	0.19
Average											6.55	0.22

B. Cats with Anoxia and Increased Carbon Dioxide Tension

93 D	60	3 hr. 26 min.	30 min.	9.6	8.3	41.6	46.8	55	150	104	6.8	0.32
95 D	72	5 hr. 11 min.	42 min.	10.2	9.5	54.7	51.6	56	131	124	7.2	0.30

On the other hand, when a cat anesthetized with pentobarbital sodium was made to breathe a nitrogen–oxygen mixture containing less than 10 per cent oxygen, there was a striking increase in the volume of the brain (table 4). The differential index of brain volume fell to an average of 6.55 per cent. As we pointed out, we do not know whether this fluid lost from the blood stream enters the interstitial spaces or causes swelling of the nerve and glial cells. An unexpected feature of the brain's tendency to swell during anoxia was the finding that maximal swelling

TABLE 5.—*Data on Cats Under Light Ether Anesthesia Breathing Room Air*

Cat	Duration of Anesthesia	Oxygen Saturation, per Cent	Carbon Dioxide Content, Volumes per Cent	Cerebrospinal Fluid Pressure			Differential Index of the Brain Volume, per Cent	Blood Content, Cc.
				Onset	Maximum	Final		
27 C	15 min.	Color good		...	...	..	9.4	....
31 C	1 hr. 50 min.	Color good		...	...	..	10.4	....
32 C	1 hr. 42 min.	Color good		...	...	..	8.0	....
82 D	3 hr. 32 min.	98.4	64.4	95	95	53	9.3	0.19
83 D	2 hr. 35 min.	95.5	51.0	98	102	68	10.0	....
84 D	2 hr. 23 min.	100.0	64.6	105	105	55	10.0	....
98 D	1 hr. 15 min.	95.5	42.8	...	...	..	....	0.30
108 D	.....	....	....	...	...	..	....	0.25
109 D	.....	....	....	...	...	..	....	0.28
Average							9.52	0.26

TABLE 6.—*Data on Cats Under Light Ether Anesthesia with Anoxia*

Cat	Duration of Anesthesia		Oxygen in Inspired Air, per Cent	Oxygen Saturation, per Cent	Carbon Dioxide Content, Volumes per Cent	Cerebrospinal Fluid Pressure			Differential Index of Brain Volume, per Cent	Blood Content, Cc.
	Total	Anoxia				Onset	Maximum	Final		
86 D	4 hr. 12 min.	36 min.	8	(Cyanosis ++++)		100	100	79	4.6	0.23
87 D	5 hr. 18 min.	50 min.	12.9	59.8	30.2	120	120	69	7.1	0.20
88 D	3 hr. 25 min.	50 min.	11.4	73.0	33.8	143	162	162	5.1	....
Average									5.6	0.215

may occur whenever the oxygen in the inspired air drops below 10 per cent and at any oxygen saturation of the arterial blood under 80 per cent. In cat 64 D there was no greater degree of swelling after a period of twenty-nine minutes in which these levels had been reduced nearly one half. Increasing the tension of carbon dioxide in the inspired air up to 10 volumes per cent does not cause any additional swelling of the anoxic brain tissue (table 4 *B*).

Differential Ratio of Brain Volume Under Ether Anesthesia.—When an intratracheal cannula and ether were used, with normal oxygen saturation of the arterial blood, the average index of brain volume in

6 cats was 9.52 per cent (table 5), compared with the normal of 10.50 per cent (table 2) for the unanesthetized animal. As in the series anesthetized with pentobarbital sodium, this apparent difference (0.98 per cent) was investigated by the method of Fisher for small series and found to be of no significance; by another method it was found to be of questionable significance.

When the etherized animal was made anoxic by breathing an atmosphere with the oxygen reduced below 13 per cent, swelling occurred as with the administration of pentobarbital sodium under similar basic conditions. These alterations in 3 cats are shown in table 6; the average differential index of brain volumes amounted to 5.6 per cent.

Differential Ratio of Brain Volume Under Nitrous Oxide Anesthesia.—When nitrous oxide was used, with which it is impossible to attain relaxation of the muscles without anoxia, swelling of the brain occurred in 2 cats which closely resembled that in the anoxic animals under anesthesia induced with pentobarbital sodium (table 7).

TABLE 7.—*Data on Cats Under Nitrous Oxide Anesthesia*

Cat	Duration of Anesthesia		Oxygen in Inspired Air, per Cent	Oxygen Saturation, per Cent	Carbon Dioxide Content, Volumes per Cent	Cerebrospinal Fluid Pressure			Differential Index of Brain Volume, per Cent
	Total	N_2O				Onset	Maximum	Final	
76 D	3 hr. 5 min.	40 min.	8.2	62.3	26.1	65	97	97	6.6
85 D	7 hr. 3 min.	42 min.	9.4	(Cyanosis +++)		102	253	207	7.3

In summarizing the effect of pentobarbital sodium and of ether on the volume of the brain there is strong evidence to show that no striking alterations in the permeability of the capillaries or in the content of intercellular or of intracellular fluid result from the action of these anesthetics of themselves. The slight apparent swelling occurring when ether is used was found not to be statistically significant, but further observations must be made to prove this point. Whenever anoxia is allowed to develop, large amounts of fluid escape from the capillaries and cause cerebral swelling sufficient to make intracranial operations difficult, if not impossible.

CONDITIONS WHICH CAUSE CEREBRAL VASCULAR ENGORGEMENT

The residual volume of blood in the brain after decapitation and drainage of the head as described on a foregoing page is remarkably constant and in a large series of cats averaged close to 0.2 cc. This held true whether decapitation was performed without an anesthetic or after the administration of pentobarbital sodium or of ether, regardless of whether the animal was normally oxygenated or anoxic. These findings

are recorded in tables 2, 3, 4, 5 and 6. The determinations were made as described under "Material and Methods."

Examination of table 8 shows that the blood content of the anoxic and of the normally oxygenated unexsanguinated brain is the same in the animal anesthetized with pentobarbital sodium as in the normal animal.[19] In an animal anesthetized with ether it runs a good 0.2 cc. higher; this is doubtless due to the vasodilator effect of ether on the pial

TABLE 8.—*Blood Contents of Unexsanguinated Brains of Cats*

		Duration of Anesthesia		Oxygen in Inspired Air, Volumes per Cent	Carbon Dioxide in Inspired Air, Volumes per Cent	Gases in Arterial Blood		
Cat	Anesthesia	Total	Special Gas Mixture			Oxygen Saturation, per Cent	Carbon Dioxide Content, Volumes per Cent	Blood Content, Cc.
69 D	None	.....	.....	(Breathed room air)		(Color good)		0.49
70 D	None	.....	.....	(Breathed room air)		(Color good)		0.57
75 D	None	.....	.....	(Breathed room air)		(Color good)		0.40
105 D	None	.....	.....	(Breathed room air)		(Color good)		0.36
77 D	Pentobarbital sodium	2 hr.	.....	(Breathed room air)		(Color good)		0.48
78 D	Pentobarbital sodium	2 hr.	.....	(Breathed room air)		(Color good)		0.42
72 D	Pentobarbital sodium and anoxia	2 hr. 1 min.	28 min.	6.4	0	32.0	22.8	0.52
73 D	Pentobarbital sodium and anoxia	2 hr. 26 min.	1 hr. 3 min.	9.3	0	81.2	....	0.39
67 D	Pentobarbital sodium and hypercapnia	4 hr. 28 min.	10 min.	80	20	100.0	77.1	1.00
96 D	Pentobarbital sodium, anoxia and hypercapnia	57 min.	31 min.	10.4	10.4	36.4	51.3	0.83
89 D	Ether	50 min.	.....	(Breathed room air)		87.0	25.4	0.70
94 D	Ether	58 min.	.....	(Breathed room air)		95.0	30.1	0.82
104 D	Ether	37 min.	.....	(Breathed room air)		(Color good)		0.52
90 D	Ether and anoxia	2 hr. 25 min.	1 hr. 1 min.	10.6	0	58	33.6	0.64

vessels, which was first measured directly by Finesinger and Cobb.[20] Fortunately, this degree of added vascular engorgement in a subject under ether is too slight (less than 1 per cent of the total volume of the brain) to be noticeable during intracranial operations. From the data recorded in table 8 it is evident that anoxia is not a cause of cerebral congestion. Hypercapnia, increase in the carbon dioxide tension, on the other hand,

19. Wolff and Lennox,[21] studying the pial vessels through a brain window, observed only a slight degree of vasodilatation accompanying extreme anoxia.

20. Finesinger, J. E., and Cobb, S.: The Cerebral Circulation: XXXIV. The Action of Narcotic Drugs on the Pial Vessels, J. Pharmacol. & Exper. Therap. **53**:1-33, 1935.

is a most effective vasodilator. This has been shown with regard to the pial vessels by Wolff and Lennox.[21] In cat 67 D after the animal had breathed a mixture of 20 per cent carbon dioxide in 80 per cent oxygen for ten minutes the volume of blood in the cerebral vessels was twice that of a normal animal.

Figure 4 has been made by combining the data from the two sets of experiments, adding the additional volume of blood in the unexsanguinated brain to the total volume of the exsanguinated brain corrected

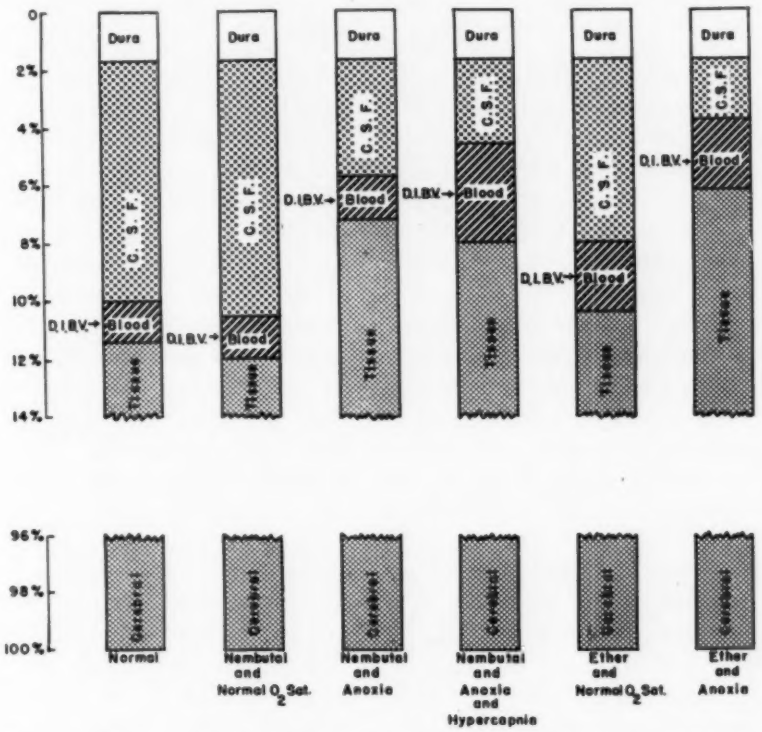

Fig. 4.—Percentage of the cranial cavity occupied by cerebral tissue, blood and cerebrospinal fluid under varying conditions. The proportion of the total blood content which remains in the exsanguinated brain is indicated by the portion which lies below the arrow marking the differential index brain volume (*D.I.B.V.*). The apparently small volume of blood in the brain is explained at least in part by the fact that the blood content of the large venous sinuses is all included in the space occupied by the dura mater.

for its residual content of blood. It is apparent that in a subject anesthetized locally as well as with pentobarbital sodium or ether, the brain

21. Wolff, H. G., and Lennox, W. G.: Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097-1120 (June) 1930.

fills approximately 91 per cent of the cranial cavity, a volume of which 89 per cent represents brain tissue and 2 per cent blood. The remaining space is filled by the dura with its large venous sinuses and the spinal fluid. The extent of the space occupied by spinal fluid which can be drained is of great importance to the neurosurgeon. In a subject under ether anesthesia with an obstructed airway, in whom both anoxia and hypercapnia are present, the brain may fill nearly the entire cranial cavity.

RELATIONSHIP OF CEREBROSPINAL FLUID PRESSURE TO BRAIN SWELLING

Changes in cerebrospinal fluid pressure in the cisterna magna were regularly observed and are tabulated in tables 3, 4, 5, 6 and 7. For convenience the alterations recorded during anoxia and hypercapnia are summarized in table 9. Examination of these readings shows that there is no correlation between the cerebrospinal fluid pressure and the degree of cerebral swelling during uncomplicated anoxia. In a certain number of these experiments there was a rapid rise in the cerebrospinal fluid pressure with the onset of anoxia, but more often than not the pressure in the final reading had fallen to a normal or near normal level. In the majority of these animals the final pressures were low. In others even the initial rises failed to take place. Furthermore, no correlation was apparent between the changes observed in spinal fluid pressure and the changes in systemic arterial blood pressure. These observations are not in accord with those of Maurer [22] or Schaltenbrand,[23] who recorded definite rises in cerebrospinal fluid pressure during anoxia. In both sets of experiments, however, the atmospheric oxygen was reduced to between 6 and 4.6 per cent. In addition to a severe degree of anoxia, Maurer employed a respiratory pump. Furthermore, the observed increases in cerebrospinal fluid pressure were noted after only brief exposure to a reduced oxygen tension. We made most of our observations with animals breathing an atmosphere of from 10 to 8 per cent oxygen and over periods of thirty minutes or longer. A few of these animals had a sharp and maintained rise in pressure (table 9). Such a response is what one might at first expect in view of the Monro-Kellie [24] hypothesis. The theory postulates that because the brain and spinal

22. Maurer, F. W.: The Effects of Anoxemia Due to Carbon Monoxide and Low Oxygen on Cerebrospinal Fluid Pressure, Am. J. Physiol. **133**:180-188, 1941.

23. Schaltenbrand, G.: Luftdruck, Kreislauf, Atmung, und Liquordruck, Acta aerophysiol. (no. 1) **1**:61-65 and 65-71, 1933; (no. 2) **1**:41-49, 1934.

24. Monro, A.: Observations on the Structure and Functions of the Nervous System, Edinburgh, Creech & Johnson, 1783. Kellie, G.: Appearances Observed in the Dissection of Two Individuals. Death from Cold and Congestion of the Brain, Tr. Med.-Chir. Soc., Edinburgh **1**:84, 1824.

cord are incompressible and enclosed in the rigid cranium and vertebral canal there can be no increase in volume of brain tissue, blood or cerebrospinal fluid without a corresponding reduction in volume of one or both of the other components. Therefore when the brain tissue swells during anoxia there must be either a displacement of cerebrospinal fluid into the manometer or a reduction in the volume of the fluid or of the intracranial blood content. Our figures on intracerebral blood volume show that this remains relatively constant during anoxia (table 8). Therefore

TABLE 9.—*Cerebrospinal Fluid Pressures of Cats Under Various Conditions*

Cat	Anesthesia	Oxygen in Inspired Air, per Cent	Carbon Dioxide in Inspired Air, per Cent	Nitrogen in Inspired Air, per Cent	Oxygen Saturation, per Cent	Carbon Dioxide, Volumes per Cent	Cerebrospinal Fluid Pressure		
							Onset	Maximum	Final
63 D	Pentobarbital sodium and anoxia	9.3	0	90.7	79.8	28.2	56	59	59
64 D	Pentobarbital sodium and anoxia	5.1	0	94.9	42.0	17.1	80	116	57
65 D	Pentobarbital sodium and anoxia	9.3	0	90.7	80.6	35.5	83	195	80
66 D	Pentobarbital sodium and anoxia	9.3	0	90.7	70.7	34.8	55	134	134
81 D	Pentobarbital sodium and hypercapnia	30.0	12.0	58.0	90.0	51.4	98	215	112
106 D	Pentobarbital sodium and hypercapnia	30.0	10.0	60.0	95.5	41.2	65	95	45
93 D	Pentobarbital sodium, anoxia and hypercapnia	9.6	8.3	82.1	41.6	46.8	55	150	104
95 D	Pentobarbital sodium, anoxia and hypercapnia	10.2	9.5	80.3	54.7	51.6	56	131	124
82 D	Ether	(Breathed room air)			98.4	64.4	95	95	55
83 D	Ether	(Breathed room air)			95.5	51.0	98	102	68
84 D	Ether	(Breathed room air)			100.0	64.6	105	105	55
86 D	Ether and anoxia	8.0	0	92.0	(Cyanosis +++)		100	100	79
87 D	Ether and anoxia	12.9	0	87.1	59.8	30.2	120	120	69
88 D	Ether and anoxia	11.4	0	88.6	73.0	33.8	143	162	162
76 D	Nitrous oxide	8.2	0	91.8*	62.3	26.1	65	97	97
85 D	Nitrous oxide	9.4	0	90.6*	(Cyanosis +++)		102	253	207

* Nitrous oxide.

it is our opinion that compensatory mechanisms come into play during prolonged periods of anoxia and that the volume of the cerebrospinal fluid is thereby reduced. These mechanisms may include (1) an increase in the rate of absorption of the fluid by the normal channels, secondary to an elevated hydrostatic pressure, (2) direct imbibition of fluid on the part of the anoxic brain tissue and (3) decreased production of cerebrospinal fluid in anoxia. According to Flexner's [25] studies, the cerebro-

25. Flexner, L. B.: The Chemistry and Nature of the Cerebrospinal Fluid, Physiol. Rev. **14**:161-185, 1934.

spinal fluid is not a dialysate but a true secretion, which means that the cells of the choroid plexus must do actual work in the formation of the fluid. This in turn necessitates an ample supply of oxygen, and the cells of the choroid plexus are most susceptible to its lack.[26]

Although we were unable to demonstrate consistent lasting elevation of the cerebrospinal fluid pressure in uncomplicated anoxia, there was a spectacular rise in the pressure when the carbon dioxide tension of the inspired air was raised. This is illustrated in table 9. In hypercapnia there is a rapid and consistent increase in intracranial pressure, which takes place concomitantly with the dilatation and congestion of the cerebral blood vessels. Although a secondary reduction was seen in some animals, the pressure rarely tended to drop back to the normal level.

COMMENT

When ether is administered by the open cone method, swelling and congestion of the brain are frequent and serious hazards for the neurosurgeon. With intratracheal cannulation obstruction of the upper part of the respiratory tract is eliminated, and this complication does not occur. The experiments described show that anoxia and increase in carbon dioxide tension are important causes of swelling and congestion of the brain. When anoxia occurs from obstruction of the respiratory tract, failure of the respiratory center or an inadequate volume of oxygen in the gas mixture (nitrous oxide), permeability of the capillaries is increased, and fluid rapidly leaves the blood stream and enters the tissues. To decide whether this transudate enters the intercellular spaces or the cells themselves is beyond the scope of this paper, but in either event it is an equal handicap to the surgeon. This loss of fluid from the capillaries is not a peculiarity of the brain but takes place unnoticed throughout the body. Maurer,[27] studying the flow of lymph from the cervical and the cardiac lymphatics in the dog, noticed that reduction of the oxygen in the inspired air causes increased production of lymph. The increase begins as the oxygen saturation of the arterial blood is lowered to 75 per cent, and it reaches a maximum at 52 per cent. With increasing deprivation of oxygen the capillary endothelium first becomes increasingly permeable to water and crystalloids, later to the larger protein molecules and finally to the red blood cells. The same is true of

26. De Meio, R. H.; Kissin, M., and Barron, E. S. G.: Studies on Biological Oxidations; on Mechanism of Catalytic Effect of Reversible Dyes on Cellular Respiration, J. Biol. Chem. **107**:579-590, 1934.

27. Maurer, F. W.: The Effects of Decreased Blood Oxygen and Increased Blood Carbon Dioxide on the Flow and Composition of the Cervical and Cardiac Lymph, Am. J. Physiol. **131**:331-348, 1940.

lymph from the lung.[28] Landis, Jonas, Angevine and Erb[29] have shown that chemical injury of the capillary endothelium may result in a sevenfold increase in the rate of fluid filtration. Acute pulmonary edema, so often seen in patients dying of head injuries and brain tumors, is probably another manifestation of increased permeability of the capillaries during anoxia.

In addition to anoxia, engorgement of the cerebral vascular bed is a second factor which may cause the brain to swell. Cerebral congestion is not related to anoxia per se (table 8) but to an increase in the tension of carbon dioxide in the arterial blood. Wolff and Lennox have shown the importance of this factor as a vasodilator of the pial vessels; its action on the cerebral vascular bed in the cat is shown by the figures for cat 67 D, which demonstrate that during extreme hypercapnia the amount of blood in the cerebral vessels became double that in the vessels of the normal brain. Hypercapnia, like anoxia, may occur in the subject under general anesthesia because of obstruction of the respiratory tract or because of respiratory failure, or it may be due to faulty construction of the closed machines used in inducing anesthesia, which may have too great a dead space or inadequate facilities for removing carbon dioxide when rebreathing is used.

In most of these experiments the effects of hypercapnia were studied separately from those of anoxia by carefully preventing any accumulation of carbon dioxide in the blood while the animals breathed atmospheres deficient in oxygen or, on the other hand, by providing adequate oxygenation while they breathed atmospheres high in carbon dioxide. However, during complications in the actual course of anesthesia both factors usually operate together and make extremely difficult an adequate exposure of deep-lying structures, such as the pituitary, the third ventricle or the cerebellopontile angle. The reduction in free intracranial space is graphically illustrated in figure 4, where the space occupied by the various substances within the cranial chamber is given in percentages of the total cranial capacity. This shows that under satisfactory conditions there is no swelling or vascular engorgement with the use of pentobarbital sodium and only a slight increase in cerebral volume with the use of ether. This increase is apparently due to a slight relaxation in vascular tone. On the other hand, when severe respiratory obstruction prevents adequate intake of oxygen and output of carbon dioxide, the brain may undergo such extreme swelling and congestion that it fills the entire space within the cranium and herniates

28. Warren, M. F., and Drinker, C. K.: The Flow of Lymph from the Lungs of the Dog, Am. J. Physiol., to be published.

29. Landis, E. M.; Jonas, L.; Angevine, M., and Erb, W.: The Passage of Fluid and Protein Through the Human Capillary Wall During Venous Congestion, J. Clin. Investigation **11**:717-734, 1932.

through an operative defect. Nitrous oxide should never be used as the sole anesthetic agent for craniotomies. To produce surgical anesthesia with this gas its concentration must often be raised to the point at which there is necessarily a drop in the oxygen saturation of the arterial blood below the critical level at which permeability of the capillaries is increased. When general anesthesia is used for intracranial operations, it is best to make routine use of the intratracheal tube. In this way obstruction of the respiratory tract can be prevented, an adequate amount of oxygen can be supplied, and carbon dioxide can be removed. If necessary to combat respiratory failure artificial respiration by intermittent insufflation of oxygen through the tube can be used. This useful device also prevents straining and elevation of intrathoracic pressure, factors which may increase the intracranial venous and capillary pressures and thereby increase bleeding from open vessels as well as cause a rise in fluid filtration from the capillary bed. The importance of this mechanism in the formation of edema has been shown by Krogh, Landis and Turner.[30]

In addition to calling attention to the value of the intratracheal tube in anesthesia for operations on the brain, our work has several other important implications. It explains the importance of adequate oxygenation of patients with head injuries when cerebral swelling is already present. Schnedorf, Munslow, Crawford and McClure[31] have shown that in experimental concussion in dogs and in cerebral injuries in human beings the oxygen saturation of the arterial blood may fall far below the critical level at which loss of fluid from the capillaries begins to take place. Nearly all the patients who died fell into this group, whereas those with an oxygen saturation above the critical level recovered. The relationship between the severity of an injury of the head and the arterial oxygen saturation is now being studied in this hospital, as is the effectiveness of oxygen therapy. The realization that reduction in the oxygen content of the inspired air is dangerous in cases of head injury has an important wartime bearing on the evacuation by airplane of persons with such injuries. Definite changes in volume of cranial contents probably begin to take place somewhere in the neighborhood of 11,000 feet, where the atmospheric oxygen is reduced to about 15 volumes per cent. At this level the arterial oxygen saturation drops to around 85 per cent in normal persons.[32] The fact that wounded soldiers tolerate badly trans-

30. Krogh, A.; Landis, E. M., and Turner, A. H.: The Movements of Fluid Through the Human Capillary Wall in Relation to Venous Pressure to the Colloid Osmotic Pressure of the Blood, J. Clin. Investigation **11**:63-95, 1932.

31. Schnedorf, J. G.; Munslow, R. A.; Crawford, A. S., and McClure, R. D.: Anoxia and Oxygen Therapy in Head Injury, Surg., Gynec. & Obst. **70**:628-631, 1940.

32. Dill, D. B.; Talbott, J. H., and Consolazio, W. V.: Blood as a Physicochemical System: Man at High Altitudes, J. Biol. Chem. **118**: 649-666, 1937.

port by air, because of the deleterious effect of anoxia on shock, is already known. When brain swelling is already present, its further increase by anoxia constitutes a serious risk.

These methods of studying volume changes which occur in the brain because of alterations in capillary permeability and because of vascular engorgement should be of value in the study and the treatment of head injuries, as well as of many other conditions which cause cerebral swelling and congestion. They are applicable to man as well as to experimental animals, although determinations made on the human brain post mortem are subject to uncontrollable errors, which have been discussed on an earlier page.

SUMMARY AND CONCLUSIONS

Quantitative methods of determining the volume and the blood content of the brain are described.

Neither swelling of tissue nor congestion of the cerebral vascular tree takes place in cats anesthetized with pentobarbital sodium provided there is an adequate airway. In cats anesthetized with ether there is no significant swelling of tissue, but there is a slight increase of blood content, due to a vasodilator effect on the cerebral vessels. This phenomenon does not appear to be sufficiently marked in man to cause any disturbance to the neurosurgeon.

From observations made on animals breathing low oxygen mixtures we conclude that anoxia results in an increase in intercellular or intracellular fluid, or both.

A rise in the carbon dioxide tension causes engorgement of the cerebral vascular tree.

If there is obstruction of the respiratory tract or respiratory failure, or if anesthetic mixtures are used with insufficient oxygen (nitrous oxide), the brain may so increase in size that intracranial operation is rendered difficult or impossible. This complication must be avoided by insuring adequate oxygenation of the tissues and by preventing an increase of carbon dioxide tension in the tissues. The intratracheal tube insures an open airway and permits the maintenance of a satisfactory supply of oxygen by insufflation if respiratory failure occurs.

This work on the behavior of the brain in anesthesia has important bearings on the treatment of patients with postoperative respiratory depression after craniotomy or cerebral trauma and on the transportation by plane at high altitude of soldiers with head injuries.

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LOCAL IMPLANTATION OF SULFANILAMIDE AND ITS DERIVATIVES IN WOUNDS

ITS RELATION TO WOUND HEALING AND TO PERITONEAL ADHESIONS

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The bacteriostatic effects of sulfanilamide and its various derivatives are now too well known to require comment, and the rationale of the local use of these drugs in wounds has recently been reviewed by Key and Frankel.[1] Consequently, in this paper no attempt will be made to review the literature either on the effects of the drugs on various types of bacteria or on whether they are of value in combating infection when used locally in wounds. It is, however, a matter of growing interest to know whether or not the introduction of these drugs will inhibit the process of wound healing or will lead to the formation of adhesions in the peritoneum. This matter becomes especially important when one considers two stage procedures within the abdominal cavity; the difficulty encountered is often dependent on the presence of firm peritoneal adhesions.

It was noted by Key and Burford [2] that the introduction of powdered sulfanilamide and its derivatives into wounds did not interfere sufficiently with the healing of the wounds to be of clinical importance. However, in their experiments the tensile strength of the wounds was not tested. Taffel and Harvey [3] introduced sulfanilamide crystals into small wounds of the stomach in a series of white rats and compared these animals with those of a series of controls on which similar operations were performed;

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1. Key, J. A., and Frankel, C. J.: The Local Use of Sulfanilamide, Sulfapyridine and Sulfamethylthiazole, Ann. Surg. **113**:284-297 (Feb.) 1941.

2. Key, J. A., and Burford, T. H.: The Local Implantation of Sulfanilamide in Compound Fractures: Its Effect on Healing, South. M. J. **33**:449-455 (May) 1940; The Prophylactic Implantation of Sulfanilamide in Clean Operative Wounds for the Reduction of Postoperative Infections, Surg., Gynec. & Obst. **73**:324-332 (Sept.) 1941.

3. Taffel, M., and Harvey, S. C.: Effect of Local Application of Sulfanilamide upon Wound Healing, Proc. Soc. Exper. Biol. & Med. **47**:202-205 (June) 1941.

they found that there was no appreciable difference in the healing of the wounds in the two series as measured by the tensile strength.

In this paper we shall report: (1) a series of observations on the tensile strength of wounds in the abdominal wall and into the stomach and the duodenum into which sulfanilamide was implanted; (2) a series of experiments in which sulfanilamide and its derivatives were introduced into the abdominal cavity in rats to determine whether the drugs tended to cause peritoneal adhesions.

EFFECT OF SULFANILAMIDE ON THE HEALING OF WOUNDS IN THE ABDOMINAL WALL AND IN THE STOMACH AND THE DUODENUM

Adult guinea pigs and white rats were anesthetized with pentobarbital sodium, and symmetric incisions were made in the abdominal wall and carried through the peritoneum on each side. The wounds were then sutured in layers. Sulfanilamide crystals were placed in the wounds on the right side after the peritoneum had been sutured; those on the left were used as controls. In the guinea pigs it was possible to suture the wounds in three layers. In the rats the peritoneum and the rectus muscles were closed with the same continuous suture. The deeper structures were sutured with no. 000 and no. 00000 catgut, and the skin was closed with silk.

At various intervals of twenty-four hours to eleven days, the animals were killed, and the wounds were tested for tensile strength. In the guinea pigs a needle was inserted into the abdominal cavity, air was forced into the peritoneum under pressure, and the pressure at which the wound disrupted was noted. In the rats a strip approximately ½ inch (1.3 cm.) wide was excised across the abdominal wall and through the wounds. The tensile strength of each wound was then tested by clamping the strip on either side of the wound and suspending the strip with a bucket attached to the lower end. The weight of the bucket was increased by adding water, and the point at which the strip of tissue ruptured was noted. Silk sutures were removed from all wounds before the test. After four days the influence of the catgut sutures could be disregarded.

Nine guinea pigs were used in the experiment, and these were killed at intervals varying from six to nine days after the operation. On inflation it was found that air was forced out of the abdominal cavity with rupture of the wounds when the pressure rose to from 40 to 320 mm. of mercury. There was no consistent difference between the wounds treated with sulfanilamide and the control wounds of the various animals. In some instances the side on which sulfanilamide had been implanted was stronger and in others the control side was stronger. The experi-

ment was not deemed satisfactory, because the wounds tended to give way gradually, and the air tended to get between the layers of the abdominal wall and because in some instances the wounds were complicated by mild infections, not sufficient to cause breaking down of the wound but tending to weaken it. Microscopic sections were made from all wounds. A few showed low grade infection, but the infection was no more frequent in the control wounds than in those in which sulfanilamide had been implanted. Microscopically there was no demonstrable difference between the wounds treated with sulfanilamide and the control wounds either in foreign body reaction or in the extent of fibroplasia.

In the 12 rats, wounds were made on each side of the abdominal wall, and then strips ½ inch (1.3 cm.) wide were excised through the wounds and tested directly for tensile strength. The strips from wounds seven or more days old supported 410 to 1,400 Gm., depending on the age of the wound. Although the average tensile strength of the control wounds was slightly greater than that of the experimental wounds, in some instances the wounds treated with sulfanilamide were stronger. Sections of these wounds also showed a few mild infections without actual suppuration, and it was felt that these infections were sufficient to alter the tensile strength. Microscopically there was no demonstrable difference between the two series of wounds. It is to be noted that under the conditions of these experiments, in which no dressing was kept on the wounds, the implantation of sulfanilamide at the time of operation did not prevent the development of stitch abscesses in the abdominal wounds.

While these experiments were not conclusive, they indicated that the presence of a moderate amount of sulfanilamide in the wound did not seriously interfere with wound healing and that after seven or nine days the wounds were as strong as those in which the sulfanilamide had not been implanted. Previously, it was felt that the sulfanilamide powder, especially if used in too large amounts, might interfere mechanically with the healing of the wounds by tending to separate the raw surfaces.

We did not extend the series to include a large number of animals, because our experience with the two aforementioned small groups convinced us that a satisfactory determination of the actual tensile strength of healing wounds could not be made in these small animals and that for such a determination a large series of larger wounds in dogs or cats would be necessary. We performed some similar experiments on rabbits and found that these also were unsatisfactory animals for this problem. However, our small number of experiments convinced us that the presence of a moderate amount of sulfanilamide in the wound did not materially affect the rate of healing or the tensile strength of the wound.

In our experiments on viscera dogs were used, because it was felt that guinea pigs and rats were too small and that the tissues were so delicate that the wounds could not be uniformly and accurately sutured.

With the dog under general anesthesia, the abdomen was opened, and incisions 3 cm. long were made in the stomach and the duodenum. These wounds were sutured in two layers with no. 00000 catgut attached to atraumatic intestinal needles. In this series 10 animals were used (20 wounds). Ten of these wounds were used as controls, and in 10 sulfanilamide powder was introduced after the mucosa had been sutured. At intervals of five to eleven days the animals were killed in pairs, the viscus was tied off, and the tensile strength of the wounds was tested by inserting a needle into the lumen of the viscus and inflating the viscus under pressure. The tension was measured in millimeters of mercury according to the technic used by Harvey.[4]

It was found that the stomach wounds ruptured at tensions of 70 to 140 mm. of mercury, while wounds in the duodenum resisted tensions of from 160 to 520 mm. of mercury. In some instances the control wounds were stronger than those in which sulfanilamide was implanted and in other instances the wounds in which sulfanilamide had been implanted were stronger than the control wounds. It was noted that there was considerable difference in the strength of the wall of the viscus of the various animals. In 4 animals the normal lower part of the duodenum was tied off, and it was found that this could be ruptured by tensions of from 400 to 500 mm. of mercury. The eleven day old wounds of both control and experimental animals tended to reach this strength. These experiments indicated that the introduction of sulfanilamide into the wound did not appreciably delay the healing or decrease the tensile strength of the wound. It was also noted in these experiments that in those animals in which sulfanilamide had been introduced there was less reaction around the wounds than was present in the control animals. A preliminary report on these experiments has been published.[5]

DO SULFANILAMIDE AND ITS DERIVATIVES CAUSE PERITONEAL ADHESIONS?

The question whether sulfanilamide and its derivatives tend to cause peritoneal adhesions was suggested by the discovery of dense adhesions in the abdomen during the second stage of a two stage procedure for resection of the cecum. Sulfanilamide powder had been inserted after the preliminary ileocolostomy. Were these adhesions due to infection or to the presence of the powdered drug? To answer this question experiments were carried out with a group of rats. With the rat under general anesthesia, the abdomen was opened and with a small blunt

4. Harvey, S. C.: The Velocity of the Growth of Fibroblasts in the Healing Wound, Arch. Surg. **18**:1227-1240 (May) 1929.

5. Harbison, S. P.: Crystalline Sulfanilamide and Wound Healing, Bull. St. Louis M. Soc. **35**:146-147 (Dec.) 1940.

curet approximately 500 mg. of sterile crystalline or powdered sulfanilamide or one of its derivatives was introduced into the abdominal cavity. The drugs were spread around the cavity by sweeping the curet back and forth; this caused a moderate amount of trauma to the viscera and to the abdominal wall and served to distribute the powder generally over the surface of the exposed viscera. The drugs used were sulfanilamide, sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole), sulfadiazine (2-sulfanilamidopyrimidine) and a mixture of two parts of sulfanilamide and one part of sulfathiazole. Ten animals were used for the study of each drug and the mixture, and 10 were used as controls. In the latter the curet was swept about the abdominal cavity without introduction of the drugs in order to produce the same amount of mechanical trauma.

In all instances the wounds healed by first intention. One animal of the group treated with sulfathiazole died on the twenty-second day from causes unknown. There were no adhesions observed at autopsy. At the end of twenty-eight days the other animals were killed. Careful examination of the peritoneal cavity showed no adhesions in any of the animals in which the drugs had been introduced into the abdominal cavity, except for an occasional filmy adhesion of the omentum to the operative wound. Similarly, there were no adhesions in the controls, except in 2 instances in which the omentum was adherent to the site of the abdominal wound. Microscopic sections of the peritoneum of some of the animals in each group were made. Study of these sections showed no difference between the control animals and the experimental animals. In all the peritoneum appeared to be normal. In a preliminary report of a study of the early peritoneal response to treatment with these powdered drugs made by smears of the exudate obtained by aspiration, Throckmorton [6] observed no specific reaction.

CONCLUSIONS

1. The local implantation of a moderate amount of sulfanilamide powder in wounds of the abdominal wall and in wounds of the stomach and the duodenum of experimental animals does not appreciably interfere with the healing of these wounds. Such wounds when tested show approximately the same tensile strength as similar wounds in which sulfanilamide and its derivatives have not been implanted.

2. The introduction of sulfanilamide, sulfathiazole, sulfadiazine or mixtures of sulfanilamide and sulfathiazole into the peritoneal cavity does not tend to cause adhesions in the rat.

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6. Throckmorton, T. D.: The Peritoneal Response to Powdered Sulfonamide Compounds, Proc. Staff Meet., Mayo Clin. **16**:423-425 (July 2) 1941.

HISTOLOGIC CHARACTER OF THE UNDESCENDED TESTIS AFTER PUBERTY

ITS SIGNIFICANCE WITH REFERENCE TO THE PERFORMANCE OF ORCHIOPEXY

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The purposes of this paper are (*a*) to make a histologic study of the undescended testis in order to arrive at a better concept of the histologic character of the testis at various ages, (*b*) to determine how long enough of the germinal epithelium survives to justify orchiopexy and (*c*) to correlate this histologic and clinical knowledge in an attempt to formulate a rational plan of treatment for older cryptorchids.

The histology of the prepubertal testis has been discussed in detail elsewhere;[1] suffice it to say here that up to puberty there are no differences discernible grossly or microscopically between the normally descended and the undescended testis. Concerning the histologic character of the postpubertal ectopic gonad there have been but few reports. Maréchal,[2] Rawlings,[3] Vidal[4] and Burghard[5] expressed their opinion that in the majority of cases the postpubertal retained testis is capable of spermatogenesis. On the other hand, Bland-Sutton[6] and Curling[7] stated that most cryptorchids are sterile. It should be said, however, that there is undeniable clinical evidence that cryptorchids may be

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1. Wangensteen, O. H.: The Undescended Testis: An Experimental and Clinical Study, Arch. Surg. **14**:663 (March) 1927; The Surgery of the Undescended Testis, Surg., Gynec. & Obst. **54**:219, 1932; The Undescended Testis: Its Fate After Satisfactory Scrotal Anchorage, Ann. Surg. **102**:875, 1935. Rea, C. E.: Functional Capacity of the Undescended Testis, Arch. Surg. **38**:1054 (June) 1939.

2. Maréchal, A., cited by Wangensteen.[1]

3. Rawlings, L. B.: The Surgical Treatment of the Incompletely Descended Testicle, Practitioner **81**:250, 1908.

4. Vidal, E.: Quelques points du traitement des ectopies testiculaires, Assoc. franç. de chir., Proc.-verb. **19**:738-745, 1906.

5. Burghard, F. F.: Operations on the Male Genital Organs, Oxford Surg. **4**:39, 1918.

6. Bland-Sutton, J.: The Value of the Undescended Testis, Practitioner **84**: 19, 1910; in discussion on Hobday, F.: Cryptorchidism in Animals and Man, Proc. Roy. Soc. Med. **17**:3, 1923.

7. Curling, T. B.: A Practical Treatise on the Diseases of the Testis, London, 1878.

fertile. Uffreduzzi [8] claimed that 10 per cent of untreated cryptorchids show evidences of fertility. However, Caulk [9] stated his belief that such fertility is short lived and seldom lasts five to ten years after puberty in untreated cryptorchids. From the reports of Coley,[10] Wangensteen, MacCollum [11] and Rea there can be no question but that cryptorchids may have spermatozoa in the semen after operation.

In a study of 51 undescended testes, Felizet and Branca [12] observed spermatogonia in 16, spermatocytes in 12 and spermatids in 2, but they never found spermatozoa. Odiorne and Simmons [13] expressed their opinion that spermatogonia and spermatocytes can be distinguished in many cases and that in only a few can spermatozoa be seen. In their examination of 9 undescended testes of adult patients, spermatozoa were found in 4; 1 patient was 30 years of age, and the other patients were 16, 16 and 20 years of age, respectively. Godard [14] studied 5 retained testes removed from patients 19 to 25 years of age. In none were there signs of spermatogenesis. In the ectopic gonads of 16 patients on whom Corner [15] performed orchidectomy no spermatozoa were seen; however, it should be mentioned that the age of an unstated number of patients was below puberty. Wangensteen stated his view that the occurrence of spermatozoa in the retained testes of young patients is decidedly unusual and that active spermatogenesis is probably never maintained. Pace [16] reviewed histologically 24 undescended testes removed at operation at the Mayo Clinic. He found that the germinal epithelium in 4 of the 5 testes removed from patients in the fourth decade of life and in 2 of the 4 testes from patients in the fifth decade was fairly

8. Uffreduzzi, O.: Die Pathologie des Hodenretention, Arch. f. klin. Chir. **101**:150, 1913.

9. Caulk, J. R.: Treatment of Undescended Testicle, Surg., Gynec. & Obst. **35**:637, 1922.

10. Coley, W. B.: The Operative Treatment of the Undescended or Maldescended Testis with Special Reference to End Results, Surg., Gynec. & Obst. **28**: 452, 1919.

11. MacCollum, D. W.: Clinical Study of the Spermatogenesis of Undescended Testicle, Arch. Surg. **31**:290 (Aug.) 1935.

12. Felizet, G., and Branca, A.: Histologie du testicule ectopique, J. de l'anat. et physiol. **34**:589, 1898; Le testicule ectopique après la puberté, Comp. rend. Soc. de biol. **50**:967, 1898; La spermatogénès dans le testicule ectopique, Compt. rend. Soc. de biol. **54**:918, 1902.

13. Odiorne, W. B., and Simmons, C. C.: Undescended Testicle, Ann. Surg. **40**:962, 1904.

14. Godard, M. E.: Etudes sur la monorchidie et la cryptorchidie, Compt. rend. Soc. de biol. **8**:315, 1856.

15. Corner, E.: The Value of the Imperfectly Descended Testis: The Advisability of Operation and the Value of Operations Performed for Its Relief, Brit. M. J. **1**:1306, 1904.

16. Pace, J. M.: The Histology and Pathologic Anatomy of the Retained Testis, Proc. Staff Meet., Mayo Clin. **10**:726, 1935.

well preserved. The locations of the testes in patients in the fourth decade of life were abdominal, inguinal, at the external ring, and just outside the external ring, respectively; the location of the 2 testes from patients in the fifth decade were the inguinal canal and just outside the external inguinal ring, respectively. Pace found that the atrophy and degeneration of the testicular tubules progressed with age in cases of ectopy.

Thus, a review of the literature reveals few complete studies in which the age of the patient, the location of the retained gonad and its histologic appearance are correlated. In fact, so fragmentary is the histology of the postpubertal testis that the whole subject can well be reinvestigated.

MATERIAL

Forty-six undescended testes from patients past puberty were available for study. The specimens were obtained from the Ancker Hospital, St. Paul, the Minneapolis General Hospital, the University Hospitals, and the department of pathology of the University of Minnesota Medical School.[17] These organs had been removed at autopsies or at operations because of atrophy, pain, suspected tumor, inability to bring the retained testis into the scrotum, large associated hydrocele or hernia. In some instances sections for biopsy taken during the course of orchiopexy at the University Hospitals were obtained; these specimens had been fixed in 10 per cent solution of formaldehyde U. S. P. and stained with hematoxylin and eosin.

The cases of undescended testis have been analyzed from the point of view of the age of the patient, the location of the undescended testis and the gross and the microscopic appearance of the testis. Since puberty in the male occurs between the ages of 13 and 15 years without regard to race, climate or individual differences,[18] only those testes obtained from patients 15 years of age or older were considered in this study. Unfortunately, in most cases there was little information concerning the gross appearance of the gonads. Microscopically, the organs were studied as to the status of the epithelium in the tubules, the degree of differentiation of the germinal cells and the amount of interstitial tissue.

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17. Dr. John Noble, pathologist of the Ancker Hospital, Dr. Nathaniel Lufkin, formerly pathologist of the Minneapolis General Hospital, and Dr. E. T. Bell, of the department of pathology of the University of Minnesota Medical School, gave me access to case histories and specimens of postpubertal ectopic testis in their files.

18. Spangaro, S.: Ueber die histologischen Veränderungen des Hodens, Nebenhodens und Samenleiters von Geburt an bis zum Greisenalter, Anat. Hefte **18**:599, 1901.

HISTOLOGIC APPEARANCE OF THE DESCENDED TESTIS AFTER PUBERTY

The adult testis consists of seminiferous tubules separated by a loose interstitium. Lining the tubules are several layers of epithelial cells. The Sertoli or nourishing cells lie directly on the basement membrane of the tubule. They take no part in the spermatogenic cycle. They are elongated, irregularly pyramidal cells with large oval nuclei rich in chromatin. Toward the periphery of the tubule and scattered between the Sertoli cells are the spermatogonia, the progenitors of the adult male sex cells. In the prepubertal testis the Sertoli cells and the spermatogonia are the only cells lining the seminiferous tubules. In the mature testis the spermatogonia are small round elements with nuclei rich in chromatin. By growth the spermatogonia become spermatocytes of the first order. These are large spherical or oval cells. The long axes of the oval cells when the latter are closely packed together are perpendicular to the basement membrane. Each of these cells divides and forms two secondary spermatocytes. The daughter cells of the secondary spermatocytes are called spermatids. The spermatids do not divide but undergo a long series of peculiar transformations before the mature spermatozoa are formed (Blom).

ANALYSIS OF DATA ON UNDESCENDED TESTES

The incidence of undescended testis in the various age groups and the location of the retained gonad in the 46 cases are given in table 1. The histologic findings in this series are recorded in table 2.

In the 46 testes studied, spermatogonia were observed in 17; primary spermatocytes, in 13; secondary spermatocytes, in 8, and spermatids, in 3. In none were spermatozoa seen. It is interesting that spermatids were seen in the undescended testes removed from patients in the third, the fourth and the seventh decades of life. The location of these testes was abdominal, inguinal or near the external ring.

The sooner after puberty the undescended testis is examined, the less degenerated is its histologic appearance. There seems to be no difference in the microscopic picture between the testis retained in the abdomen and that retained in the inguinal canal. In old cryptorchids the tubules begin to atrophy. The tubular epithelium becomes quite degenerated and consists of no more than a hyaline ring in some instances. Occasionally not even Sertoli cells can be differentiated. The amount of interstitial tissue becomes increased and more fibrous with age.

Two cases are of particular interest. In case 21 the patient was a 50 year old man who had a testis retained ½ inch (1.3 cm.) below the external ring. It is possible that this was really a high scrotal testis. It was noted that while about two thirds of the tubules were obliterated by hyaline change, in others the epithelium was fairly normal; in fact,

spermatogenic cells up to primary spermatocytes were seen. In case 43 the patient was a man 60 years old whose ectopic gonad was inguinally retained near the external ring. Microscopically, the tubules showed little atrophy. Spindle-shaped cells similar to spermatids were seen.

However, the finding of so little atrophy of the germinal epithelium in these 2 old cryptorchids seems to be the exception and not the rule. In this study it was present in only 2 of 46 cases (4.4 per cent). Similar

TABLE 1.—*Age Incidence and Location of Undescended Testis in Forty-Six Cases*

Age Incidence		Location of Testis	Side	Cases
Age Group, Yr.	Cases			
15-20	10	Abdominal	Right	9
21-30	12		Left	1
31-40	5		Unknown	2
41-50	7	Inguinal	Right	20
51-60	6		Left	2
61-70	5		Bilateral	2
71-	1		Unknown	7
		High scrotal or outside external ring (?) (cases 21 and 43).....	.....	2
		Perineal.....	.....	1

TABLE 2.—*Histologic Observations in Forty-Six Cases of Postpubertal Undescended Testis*

	Undescended Testes Showing											
Age Group, Yr.	Fairly Normal Tubules	Slightly Atrophic Tubules	Markedly Atrophic Tubules	Sertoli Cells	Spermatogonia	Primary Spermatocytes	Secondary Spermatocytes	Spermatids	Spermatozoa	Slight Increase of Interstitial Tissue	Moderate Increase of Interstitial Tissue	Marked Increase of Interstitial Tissue
15-20	5	4	1	10	8	8	4	..	..	4	6	1
21-30	2	4	5	10	5	3	2	1	..	1	4	1
31-40	..	1	4	2	1	1	1	1	..	1	..	3
41-50	1	2	6	5	2	1	1	..	..	2	1	2
51-60	1	..	3	4	2	1	1	1	..	2	..	3
61-70	1	..	3	2	..	..	..	..	..	1	2	..
71-	..	..	1	..	..	..	..	..	..	..	..	1

to the cases in the study by Pace, in which the ectopic testes removed during the fourth and fifth decades of life showed fairly well preserved germinal epithelium, the location of the gonads described in the foregoing paragraph was at or near the external ring. Moore [19] and Southam and Cooper [20] concluded that the farther the preadolescent

19. Moore, C. R.: Behavior of Testis Under Varying Experimental Conditions and Function of Scrotum: Transplantation, Cryptorchidism, Vasectomy, Minnesota Med. **7**:753, 1924.

20. Southam, A. H., and Cooper, E. R. A.: Hunterian Lecture on the Pathology and Treatment of the Retained Testes in Childhood, Lancet **1**:805, 1927.

undescended testis has descended, the more closely it corresponds to the normally located gland at the same age. My findings in old cryptorchids tend to bear out this statement.

CLINICAL STUDIES CONCERNING THE FUNCTIONAL CAPACITY OF THE UNDESCENDED TESTIS

MacCollum and Wangensteen reported the presence of spermatozoa in the semen of bilateral cryptorchids treated by orchiopexy. Patients

TABLE 3.—*Data on Seven Patients with Bilateral Ectopic Testis*

Case and Patient	Age, Yr.	Type of Ectopy	Semen: Amount Ejaculated and Date	Semen: Spermatozoa	Treatment and Date	Results of Ejaculation Test After Treatment
1 F. F.	30	Bilateral, inguinal	8 cc., 12/21/37	Absent	3,000 units of chorionic gonadotropin; 12/16/38—orchiopexy on left side	2/9/39—no spermatozoa
2 F. W.	20	Bilateral, inguinal	.....	Absent	3,000 units of chorionic gonadotropin	No spermatozoa
3 A. B.	35	Bilateral, abdominal	6 cc.	Absent	3 courses of chorionic gonadotropin, total 15,000 units; also 3 courses of testosterone propionate over eight months, 25 mg. three times per week for eight doses	No results from endocrinotherapy; 8/13/39—no spermatozoa
4 H. T.	22	Bilateral, inguinal	8 cc. 7/23/37	Absent	Course of chorionic gonadotropin and bilateral orchiopexy, treatment ending 9/3/38	1/10/39—spermatozoa present; 4/4/39—spermatozoa present; 8/6/39—spermatozoa present
5 H. R.	19	Bilateral, abdominal (congenital absence of the left testis noted at operation)	.....	.....	11/2/37—orchiopexy on right side; 3/17/38—no left testis found on exploration	5/11/28—no spermatozoa; 10/19/38—no spermatozoa; 3/13/39 no spermatozoa
6 V. H.	19	Bilateral: right, abdominal; left, inguinal	5/5/35	Absent	3,000 units of chorionic gonadotropine; bilateral orchiopexy: 5/2/35—right side; 9/20/35—left side	5/11/37—no spermatozoa; 6/38—no spermatozoa
7 L. O.	22	Bilateral, abdominal	4/27/38	Absent	Bilateral orchiopexy: 4/28/38—left side; 4/18/39—right side	8/28/38—no spermatozoa; 10/28/39—no spermatozoa

showing functional benefits from orchiopexy have been young. Rea has reported the finding of spermatozoa in the semen of 2 patients with bilateral retained testis who had never received any treatment for their anomaly. Since the ages of the treated and the untreated patients whose cases were reported in the literature happened to be about the same, one may wonder whether the treated cryptorchids might not have shown spermatozoa in the semen if they had been followed the same length of time without therapy. I have had the opportunity to study 4 bilateral cryptorchids, 21 to 35 years of age, who refused surgical treatment. One patient had had intermittent endocrinotherapy (table 3, case 3). At the

time of writing these patients have been followed for over two years, and no spermatozoa have been found in their semen. It is my experience that the cryptorchids who at first fail to show spermatozoa in their semen but who later do are those treated by orchiopexy.

For the past few years sperm counts of the ejaculated semen of patients with bilateral cryptorchidism have been made before and after treatment. In 1 of the 7 cases of bilateral ectopy I have studied since Wangensteen's report in 1935, spermatozoa have been seen in the semen after orchiopexy (table 3). This case is reported in detail because, like the case reported by Wangensteen, it presents convincing evidence of the value of orchiopexy in improving the functional capacity of the germinal epithelium of the human undescended testis.

REPORT OF A CASE

The patient when first seen was 21 years old. He had undescended testes inguinally retained and bilateral indirect inguinal hernia. A course of treatment with chorionic gonadotropin (3,000 units over a period of one month) had been given with no appreciable results. On July 23, 1937, orchiopexy was performed on the right side, and a biopsy of the testis was made. On Aug. 19, 1938, orchiopexy was performed on the left side. Biopsy of the right testis showed moderate atrophy of the tubules. Sertoli cells, two or three thick, lined the basement membrane. Except for spermatogonia no specific germinal cells were seen. Biopsies were not made at the time of scrotal thigh detachment, because it was felt that the subsequent size and function of the testis might be jeopardized.

An ejaculation test had been performed before operation, and no spermatozoa were seen. However, subsequent tests on Jan. 10, April 4 and Aug. 6, 1939, revealed occasional spermatozoa in the semen. The number has never been great, but motile forms have been seen. Certainly this patient had signs of potential if not absolute fertility.

TREATMENT OF THE UNDESCENDED TESTIS IN PATIENTS PAST PUBERTY

All surgeons agree that the testis which at puberty has failed to descend spontaneously or by endocrinotherapy should be placed in the scrotum. Up to what age the performance of orchiopexy is justified is an important question. Until about ten years ago it was thought at the University Hospitals that a cosmetic rather than functional result should be expected in patients over 17 years of age with retained testis treated by orchiopexy. Since spermatozoa have been found in the semen of patients 21 and 23 years of age, respectively, with bilateral retained testis treated by scrotal fixation, it has been felt that the indication for orchiopexy could well be extended through the third decade of life in certain cases.

With regard to cryptorchids beyond the third decade of life, one can only rationalize with knowledge in its present status, but the value of orchiopexy seems doubtful. Since in this study less that 5 per cent of the

cryptorchids past puberty showed any degree of preservation of the germinal epithelium and since the older the cryptorchid is, the greater is the testicular degeneration, it is questionable whether a functional result is ever obtained in elderly patients by orchiopexy. Then, too, the desired cosmetic result is not always obtained by scrotal fixation of the retained gland when this is of small size. In my experience the size of the retained testis is a fairly good indicator of what cosmetic and functional results may be expected. For these reasons it is my opinion that an orchidectomy rather than orchiopexy may be indicated for the majority of older cryptorchids. Certainly if there is large associated hernia, if the testis is atrophied, or if one suspects malignant growth, the testis should be removed. Only if the testis is of good size and near the external ring should orchiopexy be considered for these older patients.

SUMMARY

Forty-six retained testes from patients past puberty were available for study. The ages of the patients ranged from 15 to 73 years. Histologically, atrophy, which usually was progressive with age, was observed in all the specimens. Spermatogonia were observed in 17; primary spermatocytes, in 13, secondary spermatocytes, in 8, and spermatids, in 3. In none were spermatozoa seen. Spermatids were seen in undescended testes from persons in the third, fourth and seventh decades of life. The location of these testes was abdominal, inguinal or near the external ring. It is interesting that the germinal epithelium in 2 undescended testes from patients in the sixth and seventh decades of life was fairly well preserved. These testes had been located near the external inguinal ring.

At the University Hospitals patients with bilateral cryptorchidism up to 24 years of age have shown spermatozoa in the semen. For this reason, and because a scrotal position is necessary for continued function of the human testis, it is felt that orchiopexy may well be performed on selected patients with undescended gonads as late as the third decade of life. In older patients, in view of the small size of the testis and the degree of degeneration of the germinal epithelium, it is questionable whether a functional result is obtained by orchiopexy. In this study less than 5 per cent of the cryptorchids past puberty showed any degree of preservation of the germinal epithelium. Only if the testis is of good size and near the external ring should orchiopexy be considered for older cryptorchids.

POSTOPERATIVE INFECTIONS OF THE RESPIRATORY TRACT IN RELATION TO INHALATION AND SPINAL ANESTHESIA

A STUDY OF SIX HUNDRED AND THIRTY-ONE CASES

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The purpose of this study was to determine the relative incidence of infections of the respiratory tract after inhalation anesthesia and after spinal anesthesia in patients who had not had preoperative infections of the respiratory tract and who had undergone the same types of abdominal operations.

Since 1901 a copious literature has accumulated concerning postoperative complications involving the respiratory tract. An examination of this literature revealed that there was no previous report comparing the rates of occurrence of such complications in controlled groups of patients who had been subjected to the same abdominal operative procedures under ether, cyclopropane and spinal anesthesia.

MATERIAL AND METHOD

The material consisted of 631 cases in which abdominal operations were performed in the surgical service at Duke Hospital between the years 1930 and 1941. The operations included 245 appendectomies, 216 inguinal herniorrhaphies and 170 operations on the biliary tract, of which 166 were cholecystectomies. The cases in each operative-anesthetic group were consecutive, and in no case was a combination of inhalation and spinal anesthesia employed. The appendectomies were performed through McBurney incisions, and the operations on the biliary tract through incisions in the right rectus muscle.

Included were only those cases in which it could be determined definitely from the record that no infection of the respiratory tract existed at the time of operation. Postoperative infections of the respiratory tract were considered to have occurred only when the patients showed definite acute infections of the upper respiratory tract or pulmonary signs on physical or roentgen examination as recorded in the postoperative progress notes. The postoperative infections of the respiratory tract were classified as: (*a*) pneumonia and (*b*) nonpneumonic acute infections of the respiratory tract., e. g. acute bronchitis or coryza. The numerous subtables were omitted from this report in order to avoid confusion from an excess of charts and because they did not add materially to the study. All tables and calculations were checked by the chi square test.

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INCIDENCE OF POSTOPERATIVE INFECTIONS OF THE RESPIRATORY TRACT

In this study it was found that in patients who did not have any infection of the respiratory tract at the time of operation the incidence of postoperative infections of the respiratory tract was: after ether anesthesia 5.8 per cent, after cyclopropane anesthesia 4.9 per cent and after spinal anesthesia 7.5 per cent (table 1). That is, approximately the same proportion of patients had postoperative infections of the respiratory tract irrespective of the type of anesthesia used. Although these figures are probably small enough to make it not too markedly significant, it should be observed that the incidence after spinal anes-

TABLE 1.—*Postoperative Infections of the Respiratory Tract in Relation to the Type of Anesthesia*

	Ether			Cyclopropane *		Spinal			Totals		
	Appendectomies	Herniorrhaphies	Biliary Tract	Appendectomies	Herniorrhaphies	Appendectomies	Herniorrhaphies	Biliary Tract	Ether	Cyclopropane	Spinal
Total number of patients.....	80	73	89	87	76	78	67	81	242	163	226
Patients with postoperative infections of the respiratory tract.....	5	4	5	5	3	6	5	6	14	8	17
Percentage of patients with postoperative infections †.....	6.3%	5.5%	5.6%	5.8%	3.9%	7.7%	7.5%	7.4%	5.8%	4.9%	7.5%

* Too few operations on the biliary tract were performed under cyclopropane to be included in this study.

† This is expressed as per cent of the total number of patients in the operative-anesthetic group.

thesia was 35 per cent greater than that after cyclopropane anesthesia and 23 per cent greater than that after ether anesthesia. These same relative proportions between the types of anesthesia held in each operative-anesthetic group (table 1). There were no deaths in this series of cases.

In the literature the incidence of postoperative respiratory tract complications has been reported as varying between 1.04 per cent and 21 per cent with ether,[1] between 0 per cent and 2.07 per cent with cyclo-

1. (*a*) Gray, H. K.: Postoperative Pulmonary Complications and Postoperative Use of Trendelenburg Position, Minnesota Med. **18**:273 (May) 1935. (*b*) King, D. S.: Postoperative Pulmonary Complications: Statistical Study Based on Two Years' Personal Observation, Surg., Gynec. & Obst. **56**:43 (Jan.) 1933. (*c*) Ryan, T. J.: Hyperventilation in Abdominal Surgery, J. A. M. A. **107**:267 (July 25) 1936. (*d*) Sise, L. F.: Postoperative Pulmonary Complications: Comparison of Effect of Spinal and Ether Anesthesia, S. Clin. North

propane,[2] and between 2 per cent and 12.5 per cent with spinal anesthesia.[3] Brown and Debenham [4] reported the incidence of postoperative pulmonary complications in 63 cases in which abdominal operations were performed as 4.8 per cent with ether anesthesia and 12.5 per cent with spinal anesthesia. They stated also that in 812 cases in which operations of various kinds were performed pulmonary complications were four and twenty-nine hundredths times more frequent after spinal than after inhalation anesthesia despite the fact that the "bad risks" were done with the patients under inhalation anesthesia. Brown [5] reported in his series that the incidence of pulmonary atelectasis was greater after spinal than after any form of inhalation anesthesia. The literature contains several reports of the incidence of postoperative respiratory tract complications as being at least as great after spinal as after inhalation anesthesia.[6]

America **12**:649 (June) 1932. (*e*) Whipple, A. O.: A Study of Postoperative Pneumonitis, Surg., Gynec. & Obst. **26**:29 (Jan.) 1918. (*f*) Wiggin, S. C.: Present Status of Ether Anesthesia, Anesth. & Analg. **15**:105 (May-June) 1936.

2. Bogan, J. B.: Clinical Evaluation of Cyclopropane After Its Use in Three Hundred Surgical Anesthesias, Anesth. & Analg. **15**:275 (Nov.-Dec.) 1936. Burford, G. E.: Pulmonary Complications Following 1,333 Administrations of Cyclopropane, J. A. M. A. **110**:1087 (April 2) 1938. Moffitt, J. A., and Mechling, G. S.: Comparison of Cyclopropane with Other Anesthetics, Anesth. & Analg. **15**:225 (Sept.-Oct.) 1936. Taylor, I. B.; Bennett, J. H., and Waters, R. M.: Anesthesia at Wisconsin General Hospital: Three Year Statistical Report; Anesthetic Methods and Postoperative Respiratory Complications, ibid. **16**:198 (July-Aug.) 1937.

3. King, O. C.: Spinal Analgesia: Report of Fifteen Hundred Cases, Ann. Surg. **101**:690 (Feb.) 1935. Moore, F. R.: Report of 2,434 Spinal Anesthesias, with Special Reference to Postoperative Pulmonary Complications in One Thousand Cases, U. S. Nav. M. Bull. **31**:160 (April) 1933. Washburn, F. H.: What We Have Learned from Five Hundred Spinal Anesthesias, New England J. Med. **209**: 345 (Aug. 17) 1933. Sise.[1d]

4. Brown, A. L., and Debenham, M. W.: Postoperative Pulmonary Complications: Study of Their Relative Incidence Following Inhalation Anesthesia and Spinal Anesthesia, J. A. M. A. **99**:209 (July 16) 1932.

5. Brown, A. L.: Postoperative Pulmonary Atelectasis: Observation on Importance of Different Types of Bronchial Secretions and Anesthesia, Arch. Surg. **22**:976 (June) 1931.

6. Arnheim, E. E., and Mage, S.: Spinal Anesthesia: Analysis of Four Hundred and Ninety-Seven Cases, Ann. Surg. **93**:929 (April) 1931. Emmett, J. M.: Fourteen Hundred and Fifteen Spinal Anesthesias with Special Reference to Indications, Complications, and Mortality—with Cases Reported and Charts, Virginia M. Monthly **62**:304 (Sept.) 1935. Foss, H. L., and Schwalm, L. J.: Relative Merits of Spinal and Ether Anesthesia, J. A. M. A. **101**:1711 (Nov. 25) 1933. Houston, J. C.: Comparison of Ether, Spinal, and Cyclopropane Anesthesia, Canad. M. A. J. **40**:143 (Feb.) 1939. McKittrick, L. S.; McClure, W. L., and Sweet, R. H.: Spinal Anesthesia in Abdominal Surgery, Surg., Gynec. & Obst. **52**:898 (April) 1931. Stabins, S. J., and Morton, J. J.: Observations on Spinal Anesthesia, Ann. Surg. **91**:242 (Feb.) 1930.

FACTORS NOT INFLUENCING THE INCIDENCE OF POSTOPERATIVE INFECTIONS OF THE RESPIRATORY TRACT

Age.—In each anesthetic-age group there was an average distribution of cases (table 2). In the anesthetic groups there was no regularity in the incidence of postoperative infections of the respiratory tract (table 3), and hence the incidence could not be shown to be affected by the age of the patients. Fuller [7] reported similar findings in his study. Cleveland [8] stated that in his series 52 per cent of the post-

TABLE 2.—*Age Distribution of Patients* *

	Ether (242 Cases)		Cyclopropane (163 Cases)		Spinal (226 Cases)	
	Patients	Per Cent	Patients	Per Cent	Patients	Per Cent
0- 9 years	32	13.3	2	1.3	0	0.0
10-19 years	49	20.3	48	29.4	17	7.6
20-29 years	61	25.3	60	36.8	60	26.5
30-39 years	31	12.7	23	14.1	53	23.4
40-49 years	38	15.7	12	7.3	53	23.4
50 years and over	31	12.7	18	11.1	43	19.1

* This is expressed as per cent of the total number of patients in the anesthetic group.

TABLE 3.—*Relation Between Postoperative Infections of the Respiatory Tract and Age of Patients Studied* *

	Ether (14 Cases)		Cyclopropane (8 Cases)		Spinal (17 Cases)	
	Patients	Per Cent	Patients	Per Cent	Patients	Per Cent
0- 9 years	2	14.3	0	0.0	0	0.0
10-19 years	1	7.1	2	25.0	2	11.8
20-29 years	4	28.6	3	37.5	1	5.8
30-39 years	2	14.3	2	25.0	2	11.8
40-49 years	2	14.3	0	0.0	8	47.1
50 years and over	3	21.4	1	12.5	4	23.5

* This is expressed as per cent of the total number of patients with postoperative infections of the respiratory tract in each anesthetic group.

operative respiratory tract complications occurred in patients who were in the third and fourth decades of life. The present study revealed that a similar figure held for combinations of several other decades (table 3).

Duration of the Operative-Anesthetic Time.—Rovenstine and Taylor [9] reported that the duration of the operation was the most important

7. Fuller, C. J.: Analysis of Postoperative Pulmonary Complications Based on Cases at University College Hospital, London, in One Year, Lancet **1**:115 (Jan. 18) 1930.

8. Cleveland, M.: Further Studies in Postoperative Pneumonitis, Surg., Gynec. & Obst. **28**:282 (March) 1919.

9. Rovenstine, E. A., and Taylor, I. B.: Postoperative Respiratory Complications: Occurrence Following 7,874 Anesthesias, Am. J. M. Sc. **191**:807 (June) 1936.

factor in the development of postoperative respiratory tract complications. Fuller [7] found the duration of the operation not to be a factor in the incidence of postoperative infections of the respiratory tract. In the present 631 cases the incidence with each type of anesthesia varied relatively little between the different operative procedures, i. e. between the short (appendectomies), intermediate (herniorrhaphies) and relatively long (operations on the biliary tract) operative-anesthetic procedures (table 1).

Sex.—In this series sex could not be shown to be a factor contributing to the occurrence of postoperative infections of the respiratory tract. The incidence was not markedly greater in either sex (table 4), although it was slightly higher in females than in males in each anesthetic group. Cleveland [8] and D. King [1b] reported the incidence in their studies respectively as four times and twice as great in men as in women.

TABLE 4.—*Relation Between Postoperative Infections of the Respiratory Tract and Sex of Patients Studied* *

	Ether		Cyclopropane		Spinal	
	Male	Female	Male	Female	Male	Female
Total number of patients	142	100	130	33	122	104
Patients with postoperative infections of the respiratory tract	8	6	6	2	9	8
Per cent of patients with postoperative infections	5.6%	6.0%	4.6%	6.1%	7.3%	7.7%

* This is expressed as per cent of the total number of patients in each anesthetic-sex group.

Preoperative Complications.—The preoperative complications were considered to be those usually accepted as making the patient a possible "bad risk"—e. g., diseases of the cardiovascular system or kidneys, diabetes mellitus, peritonitis or cachexia. Of the patients with such preoperative complications the proportion in which postoperative infections of the respiratory tract developed was essentially the same in each anesthetic group; i. e., the incidence was with ether anesthesia 7.1 per cent, with cyclopropane anesthesia 7.7 per cent and with spinal anesthesia 10 per cent. Likewise, the proportion of patients with postoperative infections of the respiratory tract who had preoperative complications was not markedly greatest with any one of the three types of anesthesia: ether, 14.3 per cent; cyclopropane, 12.5 per cent; spinal, 17.6 per cent. Hence, preoperative complications were not a significant factor contributing to the incidence of postoperative respiratory tract complications.

The Kind of Spinal Anesthetic Agent and the Preoperative Medication.—The choice and the amount of spinal anesthetic agent had no effect on the incidence of postoperative infections of the respiratory tract. The incidence was relatively the same in the group of patients receiv-

ing procaine hydrochloride alone as in the group given both procaine hydrochloride and pontocaine hydrochloride. The dosage of the drugs was not a factor, since in each operative–spinal anesthetic group the patients received approximately the same amount of drug. Nor did the preanesthetic medication affect the incidence, since all 631 patients received essentially the same medication.

Blood Pressure Changes.—No estimate of the relationship between the incidence of postoperative infections of the respiratory tract and changes in blood pressure during the operation could be made in this study because it was not routine to record the blood pressure of patients given inhalation anesthesia. But when spinal anesthesia was used, the blood pressure was recorded routinely at regular intervals during the operation, and in these cases there was no correlation between changes in the blood pressure during the anesthesia and the incidence of infections of the respiratory tract postoperatively.

From the data available no explanation can be given as to the anatomic-physiologic cause of postoperative infections of the respiratory tract. Whipple [10] suggested as predisposing factors pulmonary congestion and the inhibition of normal respiratory movements resulting from the abdominal incision. Czerny [10] emphasized the role of pain in the abdominal wound as a factor in preventing sufficient aeration of the lungs and expectoration of mucus from the trachea.

SUMMARY

Six-hundred and thirty-one cases in which abdominal operations were performed under ether, cyclopropane or spinal anesthesia on patients without infections of the respiratory tract at the time of operation have been reviewed to determine the incidence of postoperative infections of the respiratory tract with each type of anesthesia. In this study certain findings appeared significant:

1. Approximately the same proportion of patients without infections of the respiratory tract at the time of operation acquired postoperative infections of the respiratory tract with inhalation and with spinal anesthesia; i. e., the incidence was with ether anesthesia 5.8 per cent, with cyclopropane anesthesia 4.9 per cent and with spinal anesthesia 7.5 per cent.

2. The incidence of postoperative infections of the respiratory tract was unaffected by the age or the sex of the patients, the length of the operative-anesthetic time, the preoperative complications, the kind or the amount of the spinal anesthetic agent, the preanesthetic medication or the blood pressure changes during the anesthesia.

10. Czerny, cited by Henle: Ueber Pneumonie und Laparotomie, Arch. f. klin. Chir. **64**:339, 1901.

PREOPERATIVE AND POSTOPERATIVE INFECTIONS OF THE RESPIRATORY TRACT IN RELATION TO INHALATION AND SPINAL ANESTHESIA

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In the preceding article [1] are reported the relative rates of occurrence of infections of the respiratory tract after ether, cyclopropane and spinal anesthesia in patients who did not have any infections of the respiratory tract at the time of operation. An examination of the literature had shown no previous report comparing the rates of incidence of preoperative and postoperative infections of the respiratory tract in relation to inhalation and spinal anesthesia. The purpose of the present study was to determine the relative incidence of acute infections of the respiratory tract after ether, cyclopropane and spinal anesthesia in patients who had been shown to have the kind of low grade, chronic preoperative infections of the respiratory tract not generally considered by surgeons to be contraindications to even elective operations.

MATERIAL AND METHOD

The material was limited to 120 cases in which abdominal operations, including appendectomies, inguinal herniorrhaphies and cholecystectomies, were performed on patients who were under the three types of anesthesia and who had been shown to have such chronic preoperative infections of the respiratory tract. The operations were performed during a ten year period, and the cases in each operative-anesthetic group were consecutive. In no case were combinations of any two of the three types of anesthesia employed.

The criteria followed in determining the existence of a low grade, chronic preoperative infection of the respiratory tract necessitated finding described in the patient's preoperative record: (*a*) exudate and injection of the tonsils, (*b*) chronic postnasal discharge or (*c*) pulmonary rales characterized as being associated with chronic bronchitis. Postoperative infection of the respiratory tract was considered to have occurred only when the patient had definite pneumonia, acute bronchitis or acute coryza, determined by physical or roentgen examination, as recorded in the postoperative progress notes.

In this study the decade of life of the patient at the time of operation, the type of abdominal operative procedure and the criteria for the postoperative infection of the respiratory tract were the same as in the previous study.[1]

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1. Lyford, J., III: Postoperative Infections of the Respiratory Tract in Relation to Inhalation and Spinal Anesthesia: A Study of Six Hundred and Thirty-One Cases, Arch. Surg., this issue, p. 35.

COMMENT

It was found in this group of patients having low grade, chronic preoperative infections of the respiratory tract that the incidence of acute postoperative infections of the respiratory tract was approximately two and one-half times as great after spinal as after inhalation anesthesia (table). Analysis of the anesthetic groups revealed that 39.5 per cent of the patients with chronic preoperative infections of the respiratory tract operated on under spinal anesthesia had acute postoperative involvement of the respiratory tract, as opposed to 13.5 per cent of those under ether anesthesia and 17.5 per cent of those under cyclopropane anesthesia (table).

The results were checked for statistical significance by the chi square test. The value of such tests was well discussed by Campbell.[2] In the present study it was found that the variation between the incidence of infections of the respiratory tract after spinal anesthesia and that after

Incidence of Postoperative Infections of the Respiratory Tract in Patients Having Low Grade, Chronic Preoperative Infections of the Respiratory Tract

	Ether	Cyclopropane	Spinal
Total number of patients	37	40	43
Patients with postoperative infections of the respiratory tract	5	7	17
Per cent of patients with postoperative infections*	13.5%	17.5%	39.5%

* This is expressed as per cent of the total number of patients in the anesthetic group.

ether anesthesia, as well as after spinal and after cyclopropane anesthesia, was markedly significant since there was approximately only 1 chance in 25 that the results stated would be altered significantly by increasing the number of cases in each anesthetic group. The relative occurrence of infections of the respiratory tract after ether and cyclopropane anesthesia did not vary widely enough to be statistically significant.

King [3] stated that his studies showed preoperative infections of the respiratory tract to have a minor role in the development of postoperative respiratory tract complications since only 18.7 per cent of his patients with postoperative respiratory tract complications had preoperative infections of the upper respiratory tract. In a previous study [1] it was found that in a group of patients without any infections of the respiratory tract at the time of operation the incidence of acute postoperative infections of the respiratory tract was 5.8 per cent after ether, 4.9 per cent after cyclopropane and 7.5 per cent after spinal anesthesia. The markedly increased incidence of infections of the respiratory tract after all three

2. Campbell, H. E.: The Statistical Method, Surgery **9**:825 (June) 1941.

3. King, D. S.: Postoperative Pulmonary Complications: Statistical Study Based on Two Years' Personal Observation, Surg., Gynec. & Obst. **56**:43 (Jan.) 1933.

types of anesthesia in the present group of patients having low grade, chronic preoperative infections of the respiratory tract suggests that low grade preoperative infections of the respiratory tract were of major importance in the development of the postoperative involvements of the respiratory tract, especially after spinal anesthesia. Whipple [4] offered as a factor predisposing to postoperative pulmonary involvement the presence of a preoperative infection of the respiratory tract.

In another series [1] it was shown that the incidence of postoperative infections of the respiratory tract was unaffected by the age or the sex of the patients, the length of the operative-anesthetic time, preoperative complications other than infections of the respiratory tract, the kind or the amount of the spinal anesthetic agent, the preanesthetic medication or the blood pressure changes during the anesthesia. The same methods of analysis applied to the present group of cases indicated that these factors did not significantly affect the incidence of postoperative infections of the respiratory tract in these patients with low grade, chronic preoperative infections of the respiratory tract.

SUMMARY

One hundred and twenty cases in which abdominal operations were performed on patients who were under ether, cyclopropane or spinal anesthesia and who had been shown to have low grade, chronic preoperative infections of the respiratory tract of the kind not generally considered contraindications to even elective operations have been analyzed to determine the relative incidence of acute postoperative infections of the respiratory tract after each type of anesthesia.

Patients having low grade, chronic preoperative infections of the respiratory tract had acute postoperative infections of this tract approximately two and one-half times as frequently after spinal as after inhalation anesthesia; i. e., the incidence was after ether anesthesia 13.5 per cent, after cyclopropane anesthesia 17.5 per cent and after spinal anesthesia 39.5 per cent.

The incidence of acute postoperative infections of the respiratory tract after each type of anesthesia in patients with low grade, chronic preoperative infections of this tract was found to be markedly greater than the incidence in a previous series of patients who had not had any preoperative infections of the respiratory tract. This finding suggests that the presence of low grade preoperative infections of the respiratory tract of the kind not generally considered contraindications to even elective operations is of sufficient significance as a factor in the development of acute postoperative infections of the respiratory tract to warrant further analysis as to the choice of anesthesia.

4. Whipple, A. O.: A Study of Postoperative Pneumonitis, Surg., Gynec. & Obst. **26**:29 (Jan.) 1918.

PRIMARY SUTURE OF THE COMMON BILE DUCT IN CHOLEDOCHOLITHIASIS

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Primary suture of the common bile duct, also called immediate choledochorrhaphy, consists of making a perfect suture of the surgical incision of the duct after having completely removed the intracholedochal concretions and after having verified the patency of the papilla of Vater.

A normal elimination of bile through the papilla of Vater with complete absence of stagnation for the first two weeks after operation is the most important requisite for healing of the incision by first intention (Walzel [1]), but this depends on patency of the papilla of Vater and on free elimination of bile after removal of the concretions. According to modern criteria, the thickness of the wall of the duct, the dilatation of the ductal lumen, the turbid aspect of the bile and the presence of gravel in the choledochal bile, as well as other minor alterations, are factors of secondary importance (Weglowski [2]) in healing of the incised common bile duct by first intention. Opinions which attributed primary importance to these alterations prevailed in the past, when primary suture of the common bile duct was done only in exceptionally rare cases. The few surgeons who found many indications for primary suture reported choleperitoneum as a frequent complication (Bernhard [3]) and advised against the operation.

Von Eiselsberg [4] and his school advised primary suture of the common bile duct, provided a drain was placed through the ampulla of Vater after dilation of Vater's papilla (Walzel). The procedure was approved by well known surgeons because of its simple technic and laudable aim (Duval [5]). I have used Duval's simple modification of the procedure only in cases in which the prognosis was favorable, namely,

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1. Walzel, P.: Zur Therapie des Choledochussteiner, Arch. f. klin. Chir. **126**: 320, 1933.

2. Weglowski, R.: Les interventions opératoires sur le cholédoque, Presse méd. **34**:1124, 1926.

3. Bernhard, F.: Die Bedeutung der Cholangiographie für Praxis und Forschung, Chirurg **9**:201, 1937; Der Dauererfolg zweizeitiger Operationen an den Gallenwegen, Beitr. z. klin. Chir. **169**:25, 1939.

4. Von Eiselsberg, cited by Walzel.[1]

5. Duval, P.: Abandon du drainage biliaire externe dans la cholédochotomie pour le drainage duodénal transvatérien par tube perdu, Bull. et mém. Soc. nat. de chir. **50**:755, 1924.

in those cases in which jaundice had recently appeared, in which there were no clinical symptoms of sepsis and in which the general condition of the patient was good (Duval and Richard [6]). Dilation of the papilla was difficult in some cases and impossible in others; in a third group, in which the patients were operated on under control of cholangiography, I observed regurgitation of the injected iodized poppyseed oil to Wirsung's duct in the first few hours after a drain was placed through the ampulla of Vater, and jaundice in the days which followed. The results showed the inadvisability of transvaterian drainage. The reflux of bile to the pancreatic duct causes some inconvenience. It is not the predominant pathogenic factor of necrotic acute pancreopathy, but clinical studies and vivisection have shown that it is important. A drain placed in Vater's ampulla probably acts like a foreign body or an impacted calculus and induces spasm of Oddi's sphincter with spasmodic predominance in the sympathicotropic lower portion of the ampulla. Dilation of Vater's papilla, on the other hand, may cause trauma to the pancreas, such as that caused by violent maneuvers used in removing calculi or impacted concretions from the terminal portion of the common bile duct. Certain conditions may result from local trauma which are propitious for the development of postoperative complications, such as pancreatic necrosis and biliary peritonitis. The aforementioned considerations prove the inadvisability of transvaterian drainage; in this connection the lack of further reports and statistics in the literature is itself significant.

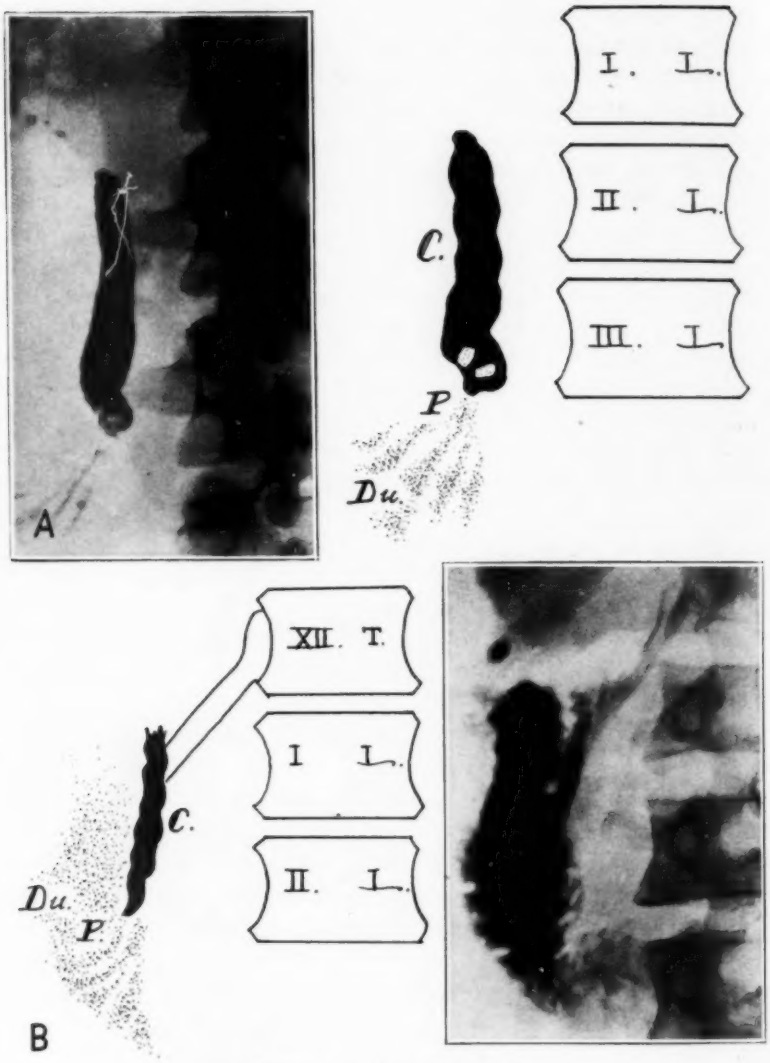
In the past the unsatisfactory results from primary suture of the common bile duct were due to the lack of proper methods for examining the patency of Vater's papilla and for determining whether all the intraductal calculi had been removed. In cases in which any of the mentioned requirements were wanting, primary suture of the common bile duct was frequently complicated by dehiscence of the incision of the common bile duct with consequent development of choleperitoneum.

INDISPENSABLE REQUIREMENTS

For primary suture of the common bile duct, the following requirements are important: (1) patency of Vater's papilla; (2) complete removal of all intraductal calculi; (3) a normal pancreas, and (4) a perfect suture of the duct.

Patency of Vater's Papilla.—The degree of patency of Vater's papilla is properly evaluated during operation by cholangiography, which actually shows whether or not there is that free course of bile to the duodenum (fig. 1) which is indispensable when primary suture of the duct is to be used. Operative cholangiography gives the same feeling of

6. Duval, P., and Richard, A.: Le drainage duodénal transvatérien par tube perdu dans la cholédochotomie, J. de chir. **26**:129, 1925.



EXPLANATION OF FIGURE 1

Fig. 1.—*A*, operative cholangiogram of a patient with secondary multiple lithiasis of the common bile duct. Iodized oil was injected into the cystic duct; the common bile duct (*C*) was somewhat dilated and uniformly injected; the nonhomogeneous portion at the lower end of the duct above the papilla (*P*) contained two small faceted calculi; some of the iodized oil passed to the duodenum (*Du*). *B*, operative cholangiogram of a patient with solitary calculus of the papilla. A concretion the size of a large pea was removed from the papilla; after this a few cubic centimeters of iodized oil was injected into the cystic duct. The lumen of the common bile duct became diminished in diameter, and the iodized oil drained freely from the duct to the duodenum. *T* and *L* signify thoracic and lumbar, respectively.

safety before primary suture of the common bile duct as it does before closure of the operative wound without drainage after cholecystectomy. The ideal cholecystectomy was discredited because of the belief that the ligation of the cystic duct might loosen with consequent development of choleperitoneum. That this is a mistaken idea was proved in my personal practice by the use of operative cholangiography in a series of 350 instances in which the wound was closed without drainage. The results revindicate the surgical tactics and the bases from which the technic was developed. The same phenomenon of revindication will be seen to apply to primary suture of the common bile duct by those who may be in doubt as to the value of the technic.

Fig. 2.—Operative cholangiogram of a patient with solitary lithiasis of the common bile duct and stenosing pancreatitis. Iodized oil (3 cc.) was injected through the cystic duct. The biliary tree was enlarged in diameter. The system of the hepatic duct (*H*) was rendered opaque. At the level of the arrow the image of the punched hollow in the common bile duct is characteristic of calculus. Some iodized oil passed through the papilla to the duodenum.

Now, primary suture of the common bile duct may be done by way of exception in the presence of a relative obstacle to the elimination of bile, provided derivation of bile is certainly feasible.

In some cases, the common bile duct, with a thin and elastic wall, contains small faceted concretions, and after these have been entirely removed, the distal portion of the duct shows a stricture at the level of the pancreas (fig. 2), or else there is delayed passage of the opaque

substance to the duodenum because of resistance of Vater's papilla. In cases of this type, if the valvular system and the caliber of the cystic duct are normal, the primary suture of the common bile duct may be complemented with a cysticoduodenostomy. This associated operation has been used under these conditions without inconvenience in 5 cases (Olmedo [7]).

Removal of Intraductal Calculi.—Total removal of the calculi from the common bile duct is easy when there is only one calculus, whereas it is difficult in the presence of many concretions. Since complete removal of the ductal concretions is necessary for primary suture of the duct, an examination of the duct is made during operation by cholangiography, which is reliable.

Normal Pancreas.—An indispensable condition to obviating external drainage is the avoidance of any possible trauma to the pancreas during operation. Caution is especially directed to the removal of calculi from the papilla of Vater and also to the removal of concretions lodged in the transpancreatic segment of the common bile duct. Violent maneuvers necessarily traumatize the pancreas with consequent development of necrosis to a greater or lesser extent in zones of the tissue. If the calculus is removed during the first maneuvers and without violence, external drainage can be avoided. If choledochotomy is difficult, the head of the pancreas is more or less traumatized; in such a case it is advisable to employ Kehr's operation.

Perfect Suture of the Duct.—Perfect suture of the common bile duct can be made when the anatomic condition of the duct is good and the proper instruments are used. In cases in which the common bile duct is papyraceous, it is advisable to make incisions no larger than necessary to allow removal of the small concretion. All laceration during the maneuvers must be avoided. As a principle, suture is proscribed when coaptation of the borders of the incision is not perfect and closure of the incision is not hermetic. The subhepatic space is always drained.

TECHNIC

The technic is based on the physiology of the hepatic duct, the integrity of which is spared during the operation. The procedure consists in supraduodenal transverse choledochotomy. Whether the operation is performed on a common bile duct with an elastic wall and a normal aspect or on a duct with a thickened wall and a dilated lumen, two loops of fine thread are used on the anterior aspect of the duct 1 cm. apart. An appropriately curved needle is used. The loops are made immediately above the duodenum along the axis of the duct. Light

7. Olmedo, F. A.: Personal communication to the author.

traction makes the anterior wall of the duct accessible to a bent bistoury, the point of which makes a transverse incision between the two loops. The incision is enlarged according to the diameter of the calculus by pushing the anterior wall of the common bile duct outward, either to the right or to the left (fig. 3). While the incision is being made, the sharp edge of the bistoury is pointed up. A small incision is generally sufficient in operations on ducts of elastic walls with small concretions. After the calculi are removed, the common bile duct is sutured with a continuous suture of no. 00 catgut. The ideal suture is that in which the stitches do not perforate; this gives a hermetic closure of

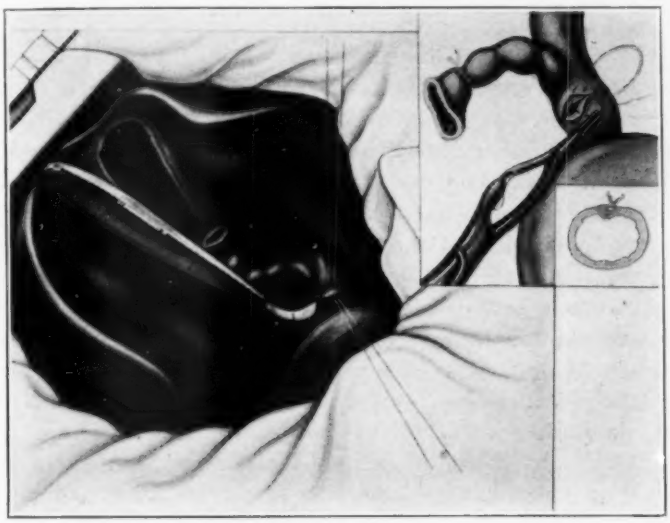


Fig. 3.—Transverse choledochotomy. The anterior wall of the common bile duct is elevated by means of two loops of thread; a transverse incision is made with a bent bistoury, and outward traction of the anterior wall of the duct is performed by means of the instrument's sharp edge and point (transfixion). The inset shows continued suture of the anterior wall of the common bile duct with nonperforating stitches.

the duct. It can generally be accomplished if the wall of the duct is thick.

As a rule, the injection of an opaque substance for examination of the route of bile elimination is made through the cystic duct, which has previously been left open for that purpose. When the cystic route cannot be used, the injection is made directly through the common bile duct just before the last stitch is taken.

OBJECTIONS

The principal objections to the procedure are the development of infection of the biliary tract and of choleperitoneum.

It is stated that the bile should be drained to prevent infection of the biliary tract. However, a simple review of the bacteriologic verifications by Elkeles [8] proves that the statement is unjustified. Infection of the biliary tract develops and evolves as long as concretions are present and stagnation of the bile obtains. The most efficient manner of controlling infection is to remove the calculi and establish a free course of the bile to the intestine. I believe that primary suture of the common bile duct has more extensive indications than those given by its advocates (Steindl [9]). Infection of the biliary tract is not a contraindication (Kirschner [10]).

In the study of the biliary apparatus, as carried on up to now in the laboratories of the Medical School of Córdola, either bile taken from the gallbladder during operation or the wall of the gallbladder was sent to the laboratory immediately after operation for bacteriologic study. Among the many investigations, the researches showing the role of the wall of the gallbladder in the development of infection of the biliary tract are of great importance. The colon bacillus and the streptococcus are the primary causal agents in the development of the infection, which evolves in the presence of various bacteria of secondary pathogenic importance.

The frequent involvement of the main route of elimination of bile in the course of cholecystitis (as verified by operative cholangiography) and the lack of bacteriologic studies of the bile of the hepatic and common bile ducts showed the need of research on the subject (Elkeles).

Observations have been made in 108 cases. In 51 cases, in addition to the bile of the gallbladder, the wall of the structure and the cystic ganglion (the material commonly obtained), the bile of the common bile duct and the contents of the duodenum also were secured. Some or all of these items in 50 cases yielded, on culture, pathogenic bacteria of given types, namely, of the colon bacillus, streptococcic, typhoid and proteus groups. These bacteria were the active agents in the production of the inflammation.

In 6 of 9 cases of supposed empyema the bile of the gallbladder was sterile; on the other hand, the gallbladder wall contained bacteria.

In 3 cases of cholecystitis the cultures made of the bile and the wall of the gallbladder, the duodenal fluid and the bile of the common bile

8. Elkeles, G.: Personal communication to the author.

9. Steindl, H.: Chirurgie der Gallenwege und dazugehörige Stoffwechselprobleme, Wien. klin. Wchnschr. **51**:920, 1938.

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duct showed colonies of typhoid bacilli. The presence of Eberthella typhi in the cultures, notwithstanding that the main route of elimination was normal, could be explained as a consequence of the fact that bile is favorable to the growth of Eberthella.

In 12 of 15 cases of calculous chronic cholecystitis the bile from the common bile duct was sterile although there were foci of infection in the neighborhood. In these 12 cases the main route of elimination of bile was free from any anatomic or functional obstacle, and the condition followed a clinical course without fever. In the remaining 3 cases in the group the choledochal bile when cultured gave scanty colonies, which seemed to be still more scanty when compared with the abundant colonies grown from material taken from other parts of the biliary tract.

The results obtained with the bile of the common bile duct in 19 cases of choledochal lithiasis are interesting. The bile of the duct was infected in 16 cases. It was sterile and of normal aspect in the 3 remaining cases in the group. The common bile duct had a thin wall and a lumen slightly increased in diameter. It was in active peristalsis. Everything seemed to indicate that the calculi had immigrated into the duct shortly before the operation.

In 9 cases in which the system of the common bile ducts did not contain calculi, the bile of the common bile duct was sterile, notwithstanding that the bile and the wall of the gallbladder and the duodenal liquid contained pathogenic bacteria. Stenosing inflammation of the sphincter of Oddi was present in 2 cases of the group, and dyskinesia (dystonia), in the other 2 cases.

Among cases recently observed, there were 2 instances of cholangiopathy without any concretions. In the first, the gallbladder was sclerotic and atrophic, the cystic duct was well preserved, stenosing pancreatitis without evident jaundice was present, and the bile of the common bile duct revealed a scanty number of bacterial colonies, though there was a great development of colonies in cultures of material from the biliary tract other than choledochal bile. In the second instance, the gallbladder was sclerotic and atrophic; it was in open communication with the main route of elimination of bile, and there was obstructive pancreatitis with an icteric syndrome of two months' duration. In this case the bile of the common duct was rich in pathogenic bacteria.

PRACTICAL DEDUCTIONS

The researches on the bacteriology of the biliary tract and of the duodenum together with the studies of the anatomic and the functional conditions of the main route of elimination of bile seem to indicate that

bile of the common duct has a great capacity for keeping free of bacteria. The observations seem to indicate that stagnation of bile due to dyskinesia and inflammation of the sphincter of Oddi is insufficient in itself to cause infection of the common bile duct. As a rule, if the concretions are allowed to remain in the common bile duct and injure its wall, calculus of the common bile duct leads to angiocholitis. Stenosing pancreatitis develops in the same manner, and the more complete the obstruction, the more acute the condition.

It is logical to suppose that the main route of bile elimination will regain its natural sterility immediately after the concretions of the hepatic and common bile ducts are removed and the mechanical factors which obstruct the free elimination of bile are eliminated. These are the fundamental considerations which justify primary suture of the common bile duct.

The common bile duct has defensive properties which make it more resistant than the other structures of the biliary tract. It has been found by vivisection to stand the action of pancreatic extracts and of colon bacilli better than the gallbladder; in fact, while the latter shows necrosis from these influences, the duct is not injured if the stagnation of the bile is suppressed in time (Brackertz [11]). The results of systematic bacteriologic studies of the bacterial flora of the biliary tree and neighboring structures prove that the bile of the hepatic and common bile ducts is sterile in the absence of lithiasis, notwithstanding the proximity of the ducts to structures involved by focal infection. Primary suture of the common bile duct has no immediate inconveniences, and the late results of the procedure are excellent. Satisfactory results from the procedure have been obtained in 31 cases, which represent approximately three fourths of the cases of choledochal lithiasis in which an operation was performed during the last four years. In summarizing I find that nowadays things have been reversed: namely, primary suture of the common bile duct is the rule; Kehr's operation is the exception (fig. 4).

One of the primary reasons for abandoning primary suture of the common bile duct was that choleperitoneum developed. This complication was due to certain factors which prevented healing and induced early dehiscence of the wound, namely, the lack of objective knowledge of the anatomic and functional conditions of the common bile duct during the operation, the frequent trauma of the pancreas during examination with instruments, the use of violent maneuvers (especially in

11. Brackertz, W.: Tierexperimentelle Untersuchungen an den extrahepatischen Gallenwegen: I. Teil; Pankreasfermentschäden, Deutsche Ztschr. f. Chir. **237**: 141, 1932; II. Teil; Infektionschäden, ibid. **240**:707, 1933.

removing calculi lodged in the distal third of the common bile duct) and the incomplete removal of the concretions. However, the conditions are now quite different, since the surgeon has objective control of the biliary tree through cholangiography during operation, by means of which the remaining calculi and the degree of patency of the terminal segment of the common bile duct are visualized. He now completes his

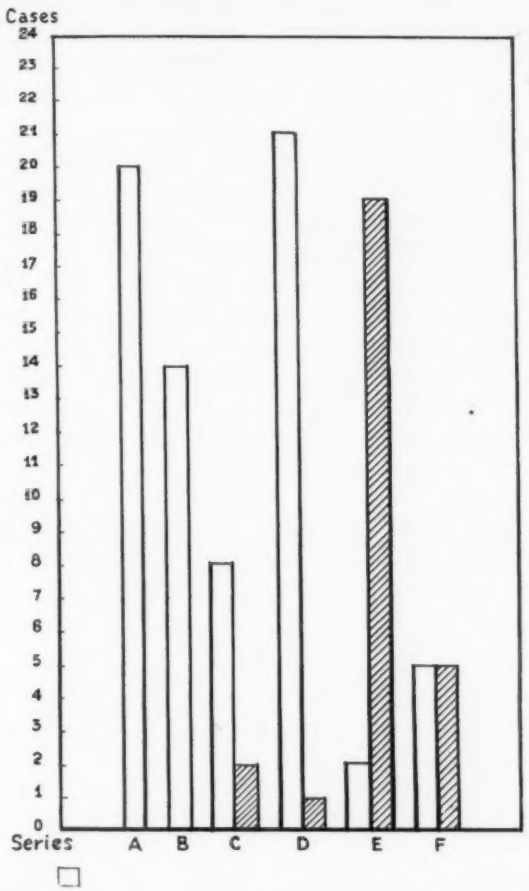

Fig. 4.—Graphic representation of the comparative frequency of Kehr's operation and of primary suture of the choledochus in several recent series of cases. The white columns signify Kehr's operation; the shaded columns represent primary suture of the choledochus.

work without interfering with the pancreas and resorts to primary suture of the common bile duct only when the synthesis of the continuity of the wound is perfect.

ADVANTAGES OF PRIMARY SUTURE

Primary suture of the common bile duct calls for thorough study of the system of the hepatic and common bile ducts, as well as for complete removal of the ductal concretions and determination of the degree of patency of the papilla of Vater.

As the elimination of bile through the intestine is reestablished, the excretory functions become normal, and the functional conditions of the liver improve. Avoiding external drainage means obviating certain disturbances which cause incomplete assimilation of food and deficient intestinal absorption of calcium (Cushny as quoted by Walters [12]), vitamins (Fromme [13]) and bile salts, with consequent development of general debility and insufficiency of organs of vital importance. Eliminating external drainage is the most effective measure for the prevention of postoperative cholerrhagia with its grave consequences, shown in the mortality rate of 64.7 per cent (Jesu [14]).

Whenever possible, placing of a tube in the duct, which is contractile and delicate, should be avoided. The indications for drainage should be diminished, and it is important that drainage should not be resorted to in patients exposed to infection and postoperative hemorrhage.

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12. Walters, W.: Obstructive Jaundice: Physiology and Surgical Aspects, Rochester, Minn., Mayo Foundation, 1931, p. 27.

13. Fromme, A.: Die Bedeutung der Vitamine für die Chirurgie, Arch. f. klin. Chir. **189**:240, 1937.

14. Jesu, Y.: La colerragia dopo drenaggio esterno delle vie biliari, Arch. ital. di chir. **44**:101, 1936.

PROPHYLACTIC INTRAPERITONEAL INTRODUCTION OF CRYSTALLINE SULFANILAMIDE

EXPERIMENTAL OBSERVATIONS

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The intraperitoneal use of crystalline sulfanilamide (powder) in the treatment of generalized peritonitis has aroused considerable interest in the past year. This is evidenced by the recent reports of Dees,[1] Thompson, Brabson and Walker[2] and Mueller,[3] all enthusiastic over the possibilities of this form of treatment. After a thirty-six year survey of the mortality from peritonitis following appendicitis, Nassau, Lorry and Pulaski[4] reported a sharp decrease in the mortality and attributed this to the use of sulfanilamide. Ravdin and his associates[5] have found a lower mortality in peritonitis associated with appendicitis since the subcutaneous use of crystalline sulfanilamide in physiologic solution of sodium chloride was instituted.

In accord with the ever increasing use of the local application of sulfanilamide in the treatment of peritonitis and other infections, we thought it advisable to determine whether sulfanilamide is as valuable in preventing peritonitis as it is in curing the disease. Rosenburg and Wall[6] recently carried out experiments in which they found that

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1. Dees, J. G.: Valuable Adjunct in Perforated Appendices (Intraperitoneal Use of Powdered Sulfanilamide), Mississippi Doctor **18**:215 (Sept.) 1940.

2. Thompson, J. E.; Brabson, J. A., and Walker, J. M.: The Intraabdominal Application of Sulfanilamide in Acute Appendicitis, Surg., Gynec. & Obst. **72**:722 (April) 1941.

3. Mueller, R. S.: Use of Powdered Crystalline Sulfanilamide in Surgery, Correspondence, J. A. M. A. **116**:329 (Jan. 25) 1941.

4. Nassau, C. F.; Lorry, R. W., and Pulaski, E. J.: Treatment of Appendicitis at Frankford Hospital: A Thirty-Six Year Survey of 4,650 Cases, Arch. Surg. **42**:296 (Feb.) 1941.

5. Ravdin, I. S.; Rhoads, J. E., and Lockwood, J. S.: Use of Sulfanilamide in Treatment of Peritonitis Associated with Appendicitis, Ann. Surg. **111**:53 (Jan.) 1940.

6. Rosenburg, S., and Wall, N. M.: The Treatment of Diffuse Peritonitis by the Direct Intraperitoneal Introduction of Sulfanilamide, Surg., Gynec. & Obst. **72**: 568 (March) 1941.

sulfanilamide powder suspended in physiologic solution of sodium chloride and injected into the peritoneal cavities of rats was of definite curative value when introduced simultaneously with a mixture of bacteria. This treatment was somewhat less valuable when the peritonitis had already been present for four to eleven hours. They suggested that the intraperitoneal route has advantages over the parenteral route but that in the human being the initial instillation must be supplemented by subsequent subcutaneous injections in order to maintain a satisfactory blood level.

In our experiments we used 108 rats and performed laparotomies on 54; we introduced the powder directly into the peritoneal cavity. This was done in order to simulate more closely the procedure carried out in the human subject. The remaining animals were used as controls.

BACTERIA USED TO PRODUCE PERITONITIS

We used a mixture of cultures of Bacterium coli and Streptococcus faecalis. The strain of B. coli was isolated from the exudate in a case of human peritonitis and was carried through three mouse passages (our preliminary experiments were carried out on mice). As the experiments with rats continued, B. coli was cultured from the dead controls and used. The strain of Str. faecalis was isolated from the stool of a human being and washed in physiologic solution of sodium chloride. This was never recultured from the dead controls, so the original strain was used throughout. Our mixture of cultures contained equal quantities of the two strains of bacteria, approximately 2,500,000,000 of each per cubic centimeter. To 10 cc. of the mixture 2 cc. of mucin was added.

METHOD

Eight rats were used to standardize the dose of the culture mixture which when injected intraperitoneally would cause the death of the animal in twenty-four hours from peritonitis. It was found that 0.5 cc. of the culture mixture would usually accomplish this end. We used on the average 300 mg. of sulfanilamide powder for each of our rats, which weighed from 150 to 250 Gm.

The first experiment consisted of introducing the culture and the sulfanilamide powder simultaneously at the time of laparotomy. In the second experiment, sulfanilamide was inserted alone, the abdomen closed and the bacteria injected intraperitoneally by needle four hours later. This would give us an evaluation of the intraperitoneal use of sulfanilamide powder as a prophylactic agent. The third experiment consisted of the simultaneous introduction of the culture and the drug and, in addition, repeated subcutaneous injections of an 0.8 per cent solution of sulfanilamide in physiologic solution of sodium chloride. The fourth experiment consisted of injecting the culture intraperitoneally by needle and performing a laparotomy for the introduction of sulfanilamide one and one-half hours later in some animals and five hours later in others. Ether anesthesia was used throughout. The abdomens were treated with alcohol before incision. A through and through silk suture was used for closure.

RESULTS

Experiment 1 (0.5 cc. of culture mixture and 300 mg. of sulfanilamide powder introduced simultaneously by laparotomy).—This procedure was carried out on 15 rats. A control series of 15 rats received an intraperitoneal injection of the same amount of the culture mixture used in the laparotomized rats, but received no sulfanilamide. Eleven of the laparotomized rats were alive and well when put to death

TABLE 1.—*Summary of Experimental Results*

	Rats Used	Rats Surviving 24 Hours	Rats Surviving 2 Weeks
Experiment 1.	Simultaneous introduction of culture mixture and sulfanilamide at laparotomy		
	15 treated animals	11 (73+%)	9 (60%)
	15 controls	3 (20%)	2 (13%)
Experiment 2.	Prophylactic introduction of sulfanilamide four hours before injection of culture mixture		
	15 treated animals	15 (100%)	11 (73+%)
	15 controls	2	2 (13.3%)
Experiment 3.	Simultaneous introduction of culture mixture and sulfanilamide followed by subcutaneous injections of sulfanilamide solution		
	12 treated animals	10 (83+%)	7 (58%)
	10 controls	0	0
Experiment 4.	Introduction of sulfanilamide after peritonitis had become established		
	6 animals treated 5 hr. after infection	2 (33+%)	1 (17%)
	6 animals treated 1½ hr. after infection	1 (17%)	1 (17%)
	6 controls	0	0

TABLE 2.—*Comparison of Survival Periods of Treated Animals*

Experiment	Percentage of Rats Alive at 24 Hours	Percentage Alive at 2 Weeks
1. Simultaneous introduction of sulfanilamide and culture mixture	73+%	60%
2. Prophylactic introduction of sulfanilamide	100%	73%
3. Simultaneous introduction of sulfanilamide and culture mixture followed by subcutaneous injection of sulfanilamide solution	83+%	58%
4. Active treatment of peritonitis with sulfanilamide		
5 hours after infection	33%	17% } 34%
1½ hours after infection	17%	17% }

two weeks after the experiment. Despite their appearance of well-being, each of these animals nevertheless had peritonitis in some degree when killed. Four of the treated animals died in twenty-four hours, 3 within forty-eight hours and 2 within seventy-two hours. Twelve of 15 controls were dead within twenty-four hours and 1 within forty-eight hours; 2 lived on apparently well.

Experiment 2 (300 mg. of sulfanilamide powder introduced intraperitoneally by laparotomy; 0.6 cc. of culture mixture injected four hours later).—This experiment was carried out on 15 rats. A control

series of 15 rats received only the injection of culture mixture. Ten of the rats operated on remained alive and were apparently well fourteen days after the experimental treatment; 2 lived forty-eight hours, and 2 lived seventy-two hours. All but 2 of the control animals were dead in less than twenty-four hours; these 2 remained alive and apparently well.

Postmortem examination revealed a seropurulent peritonitis in most of the rats. Postmortem cultures of material from all the rats yielded only B. coli.

Experiment 3 (0.6 cc. of culture mixture and 300 mg. of sulfanilamide powder introduced simultaneously; subsequent subcutaneous injections of 0.8 per cent solution of sulfanilamide in physiologic solution of sodium chloride).—This experiment was begun on 12 rats. Five cubic centimeters (40 mg.) of the sulfanilamide solution was injected subcutaneously (2.5 cc. in each flank) three times a day for two days after operation. Seven of these rats were alive and apparently well two weeks after operation; 2 lived only twenty-four hours; 2 lived forty-eight hours, and 1 lived seventy-two hours. All of the controls were dead within twenty-four hours, half of them dying within twelve hours.

Postmortem examination revealed serosanguinous or seropurulent peritonitis. Cultures yielded only B. coli.

Experiment 4 (injection of 0.5 cc. of culture mixture; laparotomy later with introduction of 300 mg. of sulfanilamide powder).—When the abdomens of the animals were opened as early as one and one-half hours after the injection of the culture mixture, there was already seropurulent generalized peritonitis. The drug was introduced in 6 rats one and one-half hours after the injection of the culture mixture and in 6 others five hours after the injection. Four in the former group and 5 in the latter group died within twenty-four hours. Only 1 in each group remained apparently well two weeks after operation. All of the control animals in this experiment were dead within twenty-four hours.

Postmortem examination revealed seropurulent peritonitis, and the cultures yielded only B. coli.

COMMENT

Sections taken from the peritoneums of rats which received only sulfanilamide powder revealed a moderate degree of edema and a mild exudative and fibroplastic reaction. Similar sections taken from rats in which starch was introduced intraperitoneally revealed a much more severe type of polymorphonuclear response. We mention this to show that sulfanilamide powder is relatively nonirritating as a foreign body when placed in the peritoneal cavity.

It is well known that the drug is readily absorbed from the peritoneum into the blood stream, so that besides its local action there is no doubt a systemic action, which in turn has its own effect on any intraperitoneal infection.

The results of experiment 2, in which sulfanilamide was placed in the peritoneal cavity four hours before the injection, indicate that the prophylactic local use of the drug has merit. A greater percentage of these animals survived than of those in any of the other experiments.

Our poorest results were obtained in experiment 4, in which the drug was introduced after the peritonitis was already existent. Our cultures were apparently more lethal than those used by Rosenburg and Wall, since most of our unprotected animals died within twenty-four hours. We were unsuccessful in saving the lives of 9 of 12 rats which had an already established peritonitis of only one and one-half to five hours' duration, while Rosenburg and Wall were able to bring about recovery in some rats in which peritonitis had been present for twenty hours. This discrepancy emphasizes the factor of variation in the virulence of the infection in cases of peritonitis from different causes, a factor making it difficult to determine accurately the value of intraperitoneal chemotherapy. The only criteria for accurate comparison are the control experiments.

As important as the virulence of the organisms is the time allowed for the infection to develop. When sulfanilamide was introduced intraperitoneally at the same time as the infection, 9 of 15 rats lived two weeks, while only 2 of 15 controls survived. When subsequent subcutaneous injections of sulfanilamide were administered, a slightly better recovery rate was observed. As stated, our results with sulfanilamide after peritonitis had become established were poor.

On the other hand, all of the rats which received a prophylactic intraperitoneal dose of sulfanilamide were alive after twenty-four hours, while all but 2 of the controls were dead. We felt that this finding was impressive enough to allow these animals to go without subsequent subcutaneous injections of the drug. As a result, 11 of 15 survived and were apparently well after two weeks.

SUMMARY

It has been known for some time that the prophylactic use of sulfanilamide and its derivatives is of great value in the prevention of severe infections in surface wounds.[7] Our experiments indicate that this principle also applies to inflammation of the peritoneum, and that the intraperitoneal use of sulfanilamide powder need not be limited to

7. Chemotherapy of War Wounds, Foreign Letters (London), J. A. M. A. **14**:1683 (April 27) 1940.

cases of active peritonitis. Our best results were obtained when sulfanilamide powder was introduced four hours before the culture mixture was injected. Our poorest results were obtained when the drug was administered after peritonitis had become established. Although our results cannot be considered conclusive, we offer the suggestion that in those cases in which there is any question of peritoneal contamination occurring during an operative procedure, it might be wise to introduce a prophylactic amount of sulfanilamide powder into the peritoneal cavity. It is comparatively nonirritating to the peritoneal surface.

The sulfanilamide powder was supplied by Eli Lilly and Company, Indianapolis.

Mr. Louis S. Cholden gave technical assistance and Dr. Katharine M. Howell guidance and advice in the preparation of this paper.

LARGE RETROPERITONEAL CHYLOUS CYST

REPORT OF A CASE, WITH EXPERIMENTS ON LYMPHATIC PERMEABILITY

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The purposes of this article are, first, to report a case of large retroperitoneal chylous cyst and, second, to advance a new explanation for the formation of a cyst of this sort on the basis of experimental work on lymphatics.

REPORT OF CASE

G. C., a white man 47 years old and a tailor by occupation, came to the Johns Hopkins Hospital with the complaint of rupture.

Previous History.—His general health had been good. There had been no abdominal symptoms except occasional postprandial eructations and moderate constipation which required the use of cathartics twice a week. There had been no jaundice or melena. When 19 years old, he had had gonorrheal infection.

Present Illness.—About seventeen years before admission, he noticed a small swelling about the size of the end of his thumb in the midline of the epigastrium. The mass gradually increased in size without producing any symptoms until five months before admission, when he had abdominal pain that persisted for four days. The pain was moderately severe, not cramplike, but constant and generalized; there was no vomiting or increase of constipation, but there was possibly some distention. He remained home for four days and then was free of any trouble until a week before admission, when he had three successive attacks of pain, about a day apart, in the upper part of his abdomen. The pain was severe and radiated to the back and to both shoulders and was present during the day. His abdomen was again apparently distended; he eructed a great deal, and it required two enemas to relieve the constipation. Vomiting occurred in only one of the attacks. He had lost about 5 pounds (2.3 Kg.) during the past year.

Physical Examination.—The patient was a well nourished and well developed Italian, 5 feet 2 inches (157.5 cm.) tall. The abdomen was protuberant, and about 6 cm. above the umbilicus there was a hernial protrusion through a ring that measured about 4 cm. in diameter. The mass was slightly tender and could not be reduced completely. It was obviously an epigastric hernia and as such could have accounted for all the symptoms. Other than this the examination yielded negative results. The blood pressure was 125 systolic and 80 diastolic.

Laboratory Data.—The white blood cell count was 9,000. The hemoglobin content was 88 per cent. The Wassermann test was negative. Examination of the urine gave negative results. Roentgen examination of the chest showed the lungs to be clear.

From the Department of Surgery, Johns Hopkins University.

Operation.—On May 3, 1932, with the patient under anesthesia induced with avertin with amylene hydrate and ether, the hernial sac was opened and found to contain besides the properitoneal fat a small amount of thin milky fluid. A culture was taken which later proved to be sterile. Palpation through the hernial ring was not satisfactory, and no pathologic growth was felt. The hernia was repaired with silk suture, and the wound healed without any complications. On May 14, the patient was examined by a medical consultant, but no pathologic process was discovered. The differential blood count was as follows: polymorphonuclear neutrophils, 81 per cent; polymorphonuclear basophils, 1 per cent; polymorphonuclear eosinophils, none; lymphocytes, 16 per cent; monocytes, 2 per cent. On May 16, a roentgen report of a flat plate of the abdomen revealed no abnormalities. A fluoroscopic examination on the following day showed no mediastinal masses; the aorta was moderately dilated; the diaphragmatic excursions were normal.

Subsequent Course.—The patient remained in good health until May 1, 1935, when he was readmitted because of distention and abdominal pain. Apparently for three months before admission he had noticed a gradual and progressive enlargement of the abdomen. At first there was no pain, nausea or vomiting. However, his appetite failed, and he felt bad generally. He had lost about 10 pounds (4.5 Kg.). No fever was noticed.

About two and a half weeks before admission he noticed a sharp constant pain in the lower part of the abdomen on the right side. There was also a mass in this region. The pain gradually increased in severity, particularly when he was in a sitting position. He obtained greatest relief by lying on his back and flexing his thighs. The mass increased in size so that it spread across the entire lower part of the abdomen, but in spite of this he was not greatly inconvenienced, since he followed his occupation until the day of admission to the hospital. There was no nausea, vomiting, constipation, diarrhea, melena or jaundice.

Physical Examination.—His temperature was 99.4 F. His pulse rate was 116 and his respiratory rate 20. The examination again yielded essentially negative results except for considerable enlargement of the abdomen. The scar from the previous operation for epigastric hernia was well healed. The abdomen was distended by a large mass which had three large lobules; one lobule was in the center, and the other two were in the right flank. The whole mass was smooth and not tender. It was possible to dislocate it a little in all directions. There was no local heat or fluctuation. The percussion note over the mass was dull. Superficial veins in the abdominal wall were not enlarged, but the veins in the legs were prominent; there was also slight pitting edema at the ankles. The blood pressure was 145 systolic and 90 diastolic.

Laboratory Data.—The white blood cell count was 6,720. The hemoglobin was 97 per cent. The differential blood cell count was normal. Roentgen studies showed a normal colon with a mass which was entirely extraintestinal. The stomach and duodenum were normal. A large cystic tumor occupied the right side of the abdomen and extended as far as the symphysis pubis.

Diagnosis.—In view of the small amount of chylous fluid observed at the previous operation, it was felt that the large mass was probably another example of chylous cyst obstruction; for that reason a diagnosis of chylous cyst was made. Echinococcic cyst was also considered a possibility.

Operation.—On May 2, with the patient under anesthesia induced by avertin with amylene hydrate supplemented with nitrous oxide and ether anesthesia, a small incision was made in the lower part of the right rectus muscle. A small amount

Fig. 1.—Roentgenogram made after patient had been given a barium sulfate meal to show how the large chylous cyst had pushed most of the small intestine into the lower left quadrant of the abdomen.

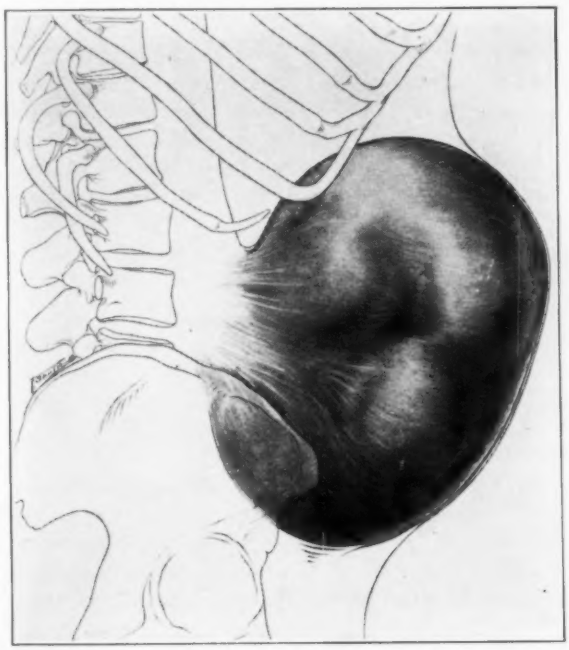

Fig. 2.—A lateral plain roentgenogram of the abdomen showed the outline of the cyst; the artist used the film to trace on the same scale the location of the cyst with reference to the bony landmarks. From observations made at the time of operation it was possible to put in the broad base and the bosses of the cyst.

of clear amber fluid escaped when the peritoneum was opened. The mass proved to be reddish gray with a smooth and glistening surface. Palpation revealed that the fluctuant mass had a large broad base the center of which was near the bifurcation of the aorta. Removal of the tumor was out of the question. All of the small intestine was pushed to the left side of the abdominal cavity, as the roentgenograms had indicated (fig. 1). After packing off the peritoneal cavity, a needle was inserted into the mass, and a thick white creamy homogeneous substance was aspirated. After the needle had been withdrawn, the white material continued to pour out through the needle hole; this indicated that the pressure in back of it was high. The needle hole was enlarged at once, and the nozzle of the aspirator was inserted into the middle of the cyst; however, the material was too thick for the small holes in the cylindric aspirator, necessitating the introduction of a simple open end tube. The cyst was then rapidly evacuated; 3,940 cc. was obtained. With the decrease in the volume of the cyst it was possible to bring its collapsed walls out of the incision and to marsupialize it with catgut sutures. A piece of the cyst wall was taken for microscopic examination. Some bleeding occurred from the inner surface of the cyst, and it was necessary to control this hemorrhage with five catgut transfixion sutures. The inside of the cyst was moderately smooth, having three depressions corresponding to the lobules. A large rubber catheter was passed to the bottom of the cyst and sutured to the mouth of the opening. In addition a Penrose drain with its gauze removed was also placed into the cavity. A petrolatum gauze pack was placed around the opening of the cyst, interrupted catgut sutures were put in the anterior rectus sheath, and the skin around the drains was approximated with interrupted silk sutures. Figure 2, drawn from a lateral preoperative roentgenogram, gives a good idea of the cyst.

The patient made an uneventful recovery, draining 50, 150, 175, 100 and 60 cc. respectively in the first five days after operation. The material was the same as that found in the cyst, only slightly thinner, and at first blood stained. At no time did his temperature exceed 99.4 F. The drains were replaced on the seventh postoperative day with a small protective wick which was allowed to remain for seventeen days.

The patient was discharged from the hospital on May 27 with a small amount of drainge which became gradually less, the wound being completely healed on June 13.

Postoperative Laboratory Reports.—Examination of the fluid from the cyst immediately after operation showed the contents to be pure fat with no cells, organisms or signs of echinococcic infection.

Examination of the histologic section of the cyst wall found it to be of varying thickness and composed essentially of dense granulation tissue, with the older fibrous tissue situated at the periphery (fig. 3). There was much round cell infiltration and an abundance of eosinophils and plasma cells. Numerous relatively large blood vessels were seen, chiefly near the lumen. A thin, fibrinous deposit covered the peritoneal surface of the cyst. The lumen had no membrane but instead showed a thick layer of fat-laden monocytes which were partly surrounded by a thin network of fibroblasts that extended a slight distance into the lumen (fig. 4). A special stain failed to show any elastic tissue in the cyst wall. The Bodian nerve stain, which was so satisfactory in other tissue work, failed to show any nerve fibers.

Diagnosis.—The diagnosis was chronic inflammatory retroperitoneal chylous cyst.

At the time of writing, the patient has been back at work six years since operation without any sign of recurrence of the cyst. Because of an attack of

slight discomfort in the upper part of the abdomen after meals, a roentgenogram of the gallbladder was taken on Jan. 27, 1940; no lesion was seen.

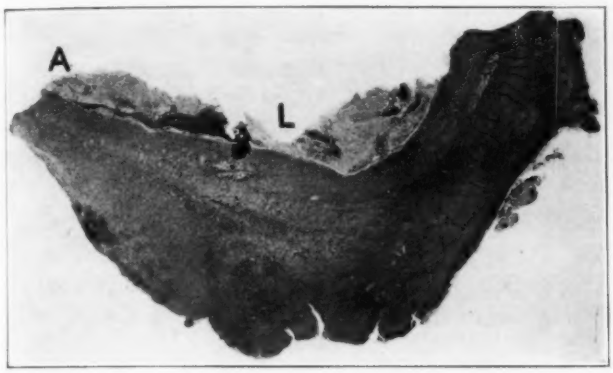

Fig. 3.—Section of the cyst wall showing the general structure and varying thickness; the dark masses in the lumen (*L*) of the cyst indicate hemorrhage; an enlargement of the area *A* is shown in figure 4.

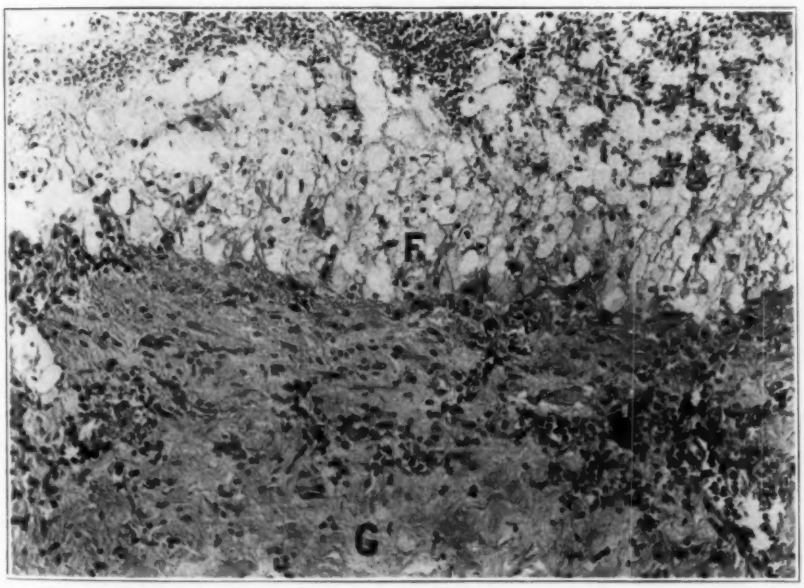

Fig. 4.—An enlargement of area *A* in figure 3 showing the granulation tissue (*G*) which composed the wall of the chylous cyst and the fat-laden monocytes (*F*) which formed the transition zone between the granulation tissue and the hemorrhagic exudate within the lumen of the cyst. There was no evidence of any lining membrane for the cyst.

COMMENT

The account of the present illness has been given in detail because the symptoms may have been due to a lesion of the abdominal lymphatic system instead of to epigastric hernia. The literature on retroperitoneal chylous cysts, with especial reference to the lymphangiomas, was summarized in 1939 by Gerster [1] in connection with a report of a case of his own. Although retroperitoneal chylous cysts are rare (only about 20 having been reported), new ones are constantly being recorded.[2] The cyst just described, containing 3,940 cc. of chyle, was one of the larger ones. It is exceeded in size only by those described by Sarwey [3] (6,200 cc.), Hadley [4] (1½ gallons [5,678 cc.]), Bonnet [5] (6,000 cc.) and Narath [6] (4,000 cc.). The unusual case of Koblanck and Pforte [7] (25 liters) was one of hydronephrosis and not of chylous cyst.

A classification of these retroperitoneal and mesenteric cysts has been made along etiologic lines by Warfield,[8] who listed the following sources: (1) embryonic retroperitoneal organs; (2) displaced embryonal intestinal tissue; (3) dermal inclusions; (4) angiomas of blood and lymph vessels; (5) necrosis of lymph nodes (e g., that in tuberculosis) or of solid tumors (e g., lipoma); (6) trauma or foreign bodies; (7) lymphatic obstruction.

In the last-named category it is proposed to put the case reported, except that it is felt that a possibly new explanation may be advanced for the formation of the cyst. It is believed that the cyst may have developed as follows: A small extravasation occurred in one of the small lymph glands near the root of the mesentery. As the chyle escaped into the retroperitoneal space, there was a reaction of the tissues so that the extravasation began to be walled off. Since, however, the rent in the wall of the lymph vessel was not closed over by a clot of

1. Gerster, J. C. A.: Retroperitoneal Chyle Cysts with Especial Reference to the Lymphangiomata, Ann. Surg. **110**:389-409, 1939.

2. Brady, L.: A Further Study of Extraperitoneal Pelvic Conditions in Women, Am. J. Obst. & Gynec. **32**:577, 1936.

3. Sarwey, O.: Ein Fall von retroperitonealer Chyluscyste bei einem 11 jährigen Mädchen: Extirpation; Heilung, Centralbl. f. Gynäk. **221**:407, 1898.

4. Hadley, M. N.: The Origin of Retroperitoneal Cystic Tumors, Surg., Gynec. & Obst. **22**:174, 1916.

5. Bonnet, cited by Speckert, J.: Ein Fall von Chyluscyste, Arch. f. klin. Chir. **75**:998, 1905.

6. Narath, A.: Ueber retropertioneale Lymphcysten, Arch. f. klin. Chir. **50**: 763, 1895.

7. Koblanck and Pforte: Hydronephrose mit chylusähnlichen Inhalt und eigenartiger Wand, nebst Bemerkungen über Chylus-Cysten, Virchows Arch. f. path. Anat. **161**:44, 1900.

8. Warfield, J. O.: A Study of Mesenteric Cysts with Report of Two Cases, Ann. Surg. **96**:329, 1932.

lymph and chyle therefore continued to flow into an area which was getting larger and which was being circumscribed more and more effectively, lymphatic mesothelium at the point of rupture was not able to seal off the defect but lined the mouth of the extravasated area and extended partly along the fibrous tissue neck of the bulbous mass without ever lining the cyst completely (fig. 4). On this basis it is understandable why a chylous cyst with a thin wall should have a mesothelial lining; such a cyst always did have a complete specialized lining and did not need granulation tissue to form an artificial wall.

The extent to which the cyst is lined by mesothelium may determine the length of time during which drainage of the marsupialized pouch may continue. If the lymphatic mesothelial cells are only at the neck of the sac, a clot will soon form and close the stoma. However, if the lining of the cyst is extensive, then chyle will continue to collect for a relatively long while, and it may be months before drainage will finally cease.

It is difficult to see how the presence of chylous fluid in these cysts can be explained on any other basis than a direct connection with chyle-bearing lymph vessels. Repeated collection of the chylous fluid after one or more aspirations would indicate such a connection.[9] The position of chylous cysts, occasionally relatively far from normal chyle channels, can be explained by an abnormal course of the lymph flow due to developmental defects or to obstruction subsequent to inflammation or tumors. That such unusual pathways for chyle occur is attested by the cases of chylous fistula, as, for instance, of the thigh,[10] of the abdomen [11] and of the scrotum.[12] It seems less likely that chyle would effuse into a preformed cystic cavity [13] or that degeneration of the wall of the cyst [14] would give rise to its extensive white fatty contents.

However, it is also difficult to explain how a rupture of a lymph vessel may occur unless one falls back on a local weakness of the vessel wall due either to a developmental defect or to a pathologic process. That the rupture may occur in the lymph gland is possible because

9. Volkmann, J.: Ueber Chyluscysten am Halse, Beitr. z. klin. Chir. **146**:654, 1929. Sarwey.[3] Hadley.[4]

10. Munk, I., and Rosenstein, A.: Zur Lehre von der Resorption im Darm nach Untersuchungen an einer Lymph (Chylus-) Fistel beim Menschen, Virchows Arch. f. path. Anat. **123**:230, 1891.

11. Fetzer, W.: Ein Fall von eigenthümlicher Erkrankung der Lymphgefässe, Arch. f. physiol. Heilk. **8**:128-132, 1849.

12. Carter, H. V.: On the Connection Between a Local Affection of the Lymphatic System and Chylous Urine, Med.-Chir. Tr. London **45**:189-207, 1862.

13. Dowd, C. N.: Mesenteric Cysts, Ann. Surg. **32**:515, 1900.

14. Henschen, K.: Beiträge zur Geschwulstpathologie des Chylusgefäss-systems, Inaug. Dissert., Zurich, 1905.

lymph nodes have been found in the walls of mesenteric cysts.[13] Experimentally, as hereinafter mentioned, such ruptures were seen to occur. Since a clinical chylous fistula of the thigh necessitates the formation of unusual lymphatic pathways and pressure relations in addition to probable congenital abnormalities or acquired pathologic processes which finally terminate in complete penetration of the relatively thick skin, it is no more difficult to believe that a relatively thin lymph vessel in the abdomen may rupture and give rise to a chylous cyst.

Symptoms.—There is as yet no symptom or group of symptoms which is pathognomonic for a retroperitoneal chylous cyst. The cysts, when small, are symptomless and are found incidentally at operation or necropsy. Only when the cysts become larger and exert pressure on contiguous structures do symptoms appear. Enlargement of the abdomen may be the first sign, followed by a loss of appetite. Pain, at first dull but constant, precedes nausea; vomiting is rare. Alternating attacks of diarrhea and constipation have been reported. Urinary frequency may appear early, but it rarely brings the patient to the physician. A slight loss of weight is common in spite of the increase in the size of the abdomen.

Diagnosis.—The diagnosis has usually been made by needle puncture. However, this method is not recommended, not only because chyle may thus escape into the peritoneal cavity but because the bowel may be punctured. The only reason the diagnosis was made in the case reported was because of the slight chylous ascites observed when the epigastric hernia was repaired. Valuable help was given by lateral roentgenograms of the abdomen, since they and not the anteroposterior views showed the smooth round character of the mass.

Briefly, some of the anomalies from which retroperitoneal chylous cyst must be distinguished and some aids to the differential diagnosis are: ovarian cyst—slow development, pelvic adhesions, menstrual disturbance, progressive weakness, dyspnea, swollen feet; pancreatic cyst—early pain in the upper part of the abdomen, not uncommonly previous cholecystitis or pancreatitis, epigastric mass (usually in the midline), abnormal appearances in roentgenograms of the intestinal tract; echinococcic cyst—slow growth, usually associated with the liver, presence of a pedicle in some instances, venous obstruction, complement fixation test; omental cyst—rarely large size, slow growth, occasional colicky pains, superficial location, movability; pedunculated myoma of the uterus—menorrhagia, bladder irritability, pain worse at menstrual periods, movable growth, usually rounded projection; hydrops of the gallbladder—location on the right side, superficial involvement, continuous with liver dulness; retroperitoneal tumor—commonly sarcoma, nodular type, deep location, loss of weight, ascites, metastases; enlargement of the

spleen—gradual protrusion from under the left costal margin, early pain from adhesions, blood abnormalities; neoplasm of the bowel—relatively small size, paroxysmal pain, blood in the stool, loss of weight, pathologic roentgen findings; movable kidney—pain radiating to the bladder, radial displacement, pathologic urinary findings, pyelographic evidence; hydronephrosis—intermittent pain, disappearing tumor, pyelographic evidence; tuberculous abscess—tuberculous infection elsewhere, slow onset, location in upper part of the abdomen, fever, weakness, loss of weight, possibly spinal caries; pregnancy.

Of the complications that have occurred with chylous cysts, the most serious has been intestinal obstruction due to volvulus, adhesions or simple mechanical compression. The mortality in such cases, usually involving resection of a part of the intestine, has been given as 50 per cent. Rupture of the cyst is rare and usually due to trauma. A malignant change in the cyst wall has been mentioned.[15]

Treatment.—The best treatment is excision if it is possible. Marsupialization has been successful in those instances in which operative removal was not possible, and even with this conservative method the mortality has been put at 16 per cent.[16] Aspiration, obviously, has no curative value.[17]

EXPERIMENTS

If the chylous cysts are formed because of lymphatic obstruction, experimental obstruction might give rise to the formation of such cysts. However, in cats and dogs cysts were never formed either after ligation of the thoracic duct in the chest [18] or subsequent to much more elaborate measures taken to obstruct the flow of lymph.[19] The measures included not only ligation of the thoracic duct in the chest but also ligation of both lymph ducts in the neck, subtotal removal of the cisterna chyli, ligation of the superior vena cava and multiple injections of sodium morrhuate in and about the lymph trunks.

Since obstruction did not produce cysts, it seemed possible that the production of a great many openings and sections of lymph trunks in

15. Hertzler, A. E.: Disease of Peritoneum, in Graham, E. A.: Surgical Diagnosis by American Authors, Philadelphia, W. B. Saunders Company, 1930, vol. 2, p. 589.

16. Roller, C. S.: Mesenteric Cysts: A Brief Discussion and Report of Three Cases, Surg., Gynec. & Obst. **60**:1128, 1935.

17. Slocum, M. A.: Surgical Treatment of Chylous Mesenteric Cysts by Marsupialization, Am. J. Obst. & Gynec. **41**:464, 1938.

18. Lee, F. C.: The Establishment of Collateral Circulation Following Ligation of the Thoracic Duct, Bull. Johns Hopkins Hosp. **33**:21, 1922.

19. Blalock, A.; Robinson, C. S.; Cunningham, R. S., and Gray, M. E.: Experimental Studies on Lymphatic Blockage, Arch. Surg. **34**:1049 (June) 1937.

order that the young regenerating lymphatic endothelium would not be strong enough in closing over the defects to resist the endolymphatic pressure might give rise to a cystic formation.

To that end the thoracic duct in each of 5 cats was ligated in the chest; in addition the intestinal lymph trunks together with the mesenteric lymph gland and all the other smaller lymph glands situated nearer the intestine were removed from the duodenum to the colon. Except for the presence of chylous ascites which persisted for the first three days, the animals showed no ill effects; and when they were killed from two weeks to two months after operation, no cysts were seen. The collateral lymph circulation which had developed was mainly an enlargement of the fine lymph plexus which accompanied the mesenteric vessels. Apparently all the openings in the lymph system caused by the operative intervention were sealed off by thrombosis.

Another method was tried. In 1932, Drinker and Field [20] reported that when the pressure was raised on a graphite suspension which was being injected into a lymph vessel of the frog's tongue, extravasations were seen to occur, indicating a rupture of the vessel wall.

To repeat, in a measure, this type of experiment, the thoracic duct was ligated in 11 cats and 1 dog and then either one hour to twenty-four hours later, with the animals under intratracheal ether anesthesia, the mesenteric lymph vessels were injected either with india ink or with a 3 per cent aqueous solution of trypan blue. In addition, in 4 animals under ether anesthesia whose thoracic ducts had not been ligated, the lymph trunk was clamped at the mesenteric gland after the injection of india ink had been started; thus an obstruction was produced between the gland and the site of injection. In only 3 instances did a definite rupture of the lymph vessel with extravasation occur.

The first example occurred in a cat whose thoracic duct had been ligated in the chest twenty-four hours before. As the trypan blue solution was being injected through a no. 27 gage needle attached to a 10 cc. syringe, a small by-pass to the main channel filled and suddenly ruptured, causing the trypan blue to extravasate between the leaves of the mesentery. It was not possible to determine the pressure that was exerted on the injected fluid within the vessel, but at best the pressure of a stream of fluid from the end of a no. 27 gage needle must of necessity be relatively small.

The second rupture was noticed under similar conditions except that commercial india ink was used. In this case a subsurface lymph vessel in the mesenteric lymph gland ruptured and gave rise to a large extravasation.

The lymph gland was also the site for the third rupture. In this instance a dog was used whose thoracic duct had been ligated in the chest one hour before. The injected mass was commercial india ink which had been dialyzed against solution of sodium chloride.

Finally, it was noticed that while trypan blue or india ink was being injected into the mesenteric lymphatics with the thoracic duct ligated occasionally the junction point where a vessel divided or was joined by a collateral vessel would become larger, like a small bay, and that some of the ink particles would work

20. Drinker, C. K., and Field, M.: The Lymph Capillaries in the Web of the Frog, Am. J. Physiol. **100**:642-649, 1932.

their way through the vessel wall and lodge in the perivascular tissue without causing a definite rupture. The phenomenon of permeation of the lymph vessel wall without rupture by a relatively large particle like india ink was commonly seen in the mesenteric lymphatics when the pressure on the injected fluid was raised and maintained for a few minutes, the thoracic duct having been previously ligated.

SUMMARY

A case in which a large retroperitoneal chylous cyst was correctly diagnosed and the patient successfully treated by marsupialization is reported. A new explanation for the formation of a thick-walled chylous cyst is advanced, namely, that the cyst forms when a chyle-bearing lymph vessel is ruptured and the extravasation of the chyle is limited by the formation of a wall of granulation tissue.

In experiments on animals, a high degree of obstruction to the lymph flow was produced, but there was no production of cysts. However, in 3 animals rupture of a small lymph vessel was directly observed while material was being injected into the lymph channel. This supports the view that the wall of a lymph vessel may rupture and that a chylous cyst may develop from the extravasation. The relative ease with which carbon particles may traverse the wall of a lymph vessel without causing rupture was also observed.

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TOTAL GASTRECTOMY

INDICATIONS FOR OPERATION WITH A REPORT OF FOUR CASES

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Total gastrectomy is no longer a surgical curiosity, but because of its technical difficulties it may never become commonplace. Relatively few patients are encountered in whom the indications for the operation accepted at present are fulfilled. These indications are: first, disease of the stomach endangering life; second, such extensive involvement of the stomach that nothing short of total gastrectomy will serve to eradicate the disease, and third, confinement of the disease to the stomach alone. The practicability of the operation is determined by the mobility of the stomach and the esophagus and by the general condition of the patient. A malignant neoplasm of the stomach is ordinarily the only disease which necessitates total gastrectomy.

The anatomy of the stomach is such that the organ offers a ready path for the spread of malignant cells from each part to every other part. The muscular distribution, the vascular channels, the lymphatic pathways and the tissue spaces all contribute their part to the permeation of carcinoma through the stomach. The pathologist in performing necropsy on patients who have succumbed to operation and in examining specimens removed by the most radical subtotal gastrectomy frequently has the experience of demonstrating malignant cells in the stomach far beyond the grossly evident borders of a given tumor. In other words, no matter how wide a margin the surgeon may believe he is providing in performing radical subtotal gastrectomy he still may leave microscopically demonstrable tumor which will eventually cause local recurrence and possibly metastasis of the original tumor.

Although Livingston and Pack [1] in their monumental statistical study of the end results of the treatment of gastric cancer demonstrated remarkably good results of subtotal gastrectomy in the hands of the most capable surgeons, there is still much room for improvement, even in the treatment of readily resectable carcinoma. Livingston and Pack showed that patients with carcinoma of the stomach when operated on by the average or occasional surgeon fare badly. Not only the operative

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1. Livingston, E. M., and Pack, G. T.: End Results in the Treatment of Gastric Cancer, New York, Paul B. Hoeber, Inc., 1939.

mortality rate but also the end results of the average surgeon have shown little or no improvement since the early days of gastric surgery around 1880.

Disregarding for the moment the cause of the high operative mortality, it is probable that in terms of end results the difference between the subtotal gastric resection of the expert gastric surgeon and that of the surgeon who performs gastrectomy only infrequently is largely one of the amount of tissue removed. Gastrojejunostomy may be much more difficult when only a little of the stomach remains, especially if exposure is difficult because of poor anesthesia, inexpert assistance or other factors that may plague the occasional operator. Widespread removal of adjacent lymph glands and lymphatics also is essential for good prognosis. The expert accomplishes it as a matter of course; the inexpert surgeon for various reasons frequently neglects it.

In all patients surviving the operation itself, excluding those who die soon of natural causes or intercurrent trouble, the failure to obtain a long time cure results either from recurrence of the tumor locally or regionally or from metastasis to some distant site. Certainly local recurrence in the remaining part of stomach or the reappearance of tumor in the regional lymph glands and lymphatics or in other adjacent structures is much more frequent than distant metastasis. Ewing [2] stated: "Recurrences [after operation] are chiefly in liver, peritoneum, and retroperitoneal nodes." In 20 consecutive instances of known recurrence in my own cases this statement was borne out. In addition, however, 4 patients were shown to have recurrent cancer in the stump of the stomach although radical subtotal gastrectomy had been performed. Therefore, the more radical the operation in terms of removal of the stomach itself and of the adjacent lymph glands and lymphatics, the greater protection there must be against recurrence. If this thought is carried to its logical conclusion, removal of the entire stomach, and the consequent opportunity to remove the greatest amount of adjacent lymph glands and lymphatics, should be the ideal surgical procedure.

Total gastrectomy, although theoretically an ideal procedure, has one distinct drawback in that the loss of the entire stomach means the loss of the so-called intrinsic factor contained in gastric secretion and related to the maintenance of a normal number of red cells in the circulating blood. Anemia of the primary type has developed in some patients who have had the entire stomach removed. However, the administration of extract of liver seems to combat the anemia, and it should prolong life indefinitely, as it does in cases of ordinary primary

2. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 720.

anemia. Yet because in the recorded cases in which total gastrectomy was done the patient has never lived longer than four and a half years,[3] there has been no opportunity to verify the efficacy of this treatment with certainty.

There are other practical obstacles to the more common performance of total gastrectomy. Operative mortality represents a major obstacle. Even subtotal gastrectomy as practiced by the average surgeon is attended by a high operative mortality. Livingston and Pack stated:

> The present resection mortality in surgical centers performing large numbers of [subtotal] gastrectomies for cancer averages seventeen per cent while that for the casual surgeon or in clinics reporting small numbers of resections is found to average approximately thirty per cent. They stated further: No surgeon who is unqualified . . . has the moral right to operate on a patient with gastric carcinoma.

More frequent performance of total gastrectomy if attempted by the average surgeon would no doubt result in a staggeringly high mortality rate. The operative mortality would certainly be higher for total gastrectomy done by the trained gastric surgeon than for subtotal gastrectomy, but just how much higher unfortunately cannot be predicted. No large series of total gastrectomies has been recorded. In the few cases reported by any one surgeon the technic of the operation has varied with the surgeon and with the individual patient. While the operative mortality in the recorded cases has been relatively high, it must not be overlooked that in almost all the cases the surgical risk has been of the highest with such extensive tumors that every factor in the case was conducive to a high immediate mortality rate as well as to a high morbidity rate.

In 1937 Allen[4] reported 15 cases of total gastrectomy; 5 were his own, and in 10 the operation was performed by eight of his associates. Eight of the 15 patients survived the operation. Of 7 patients operated on according to his finally evolved technic, 6 survived. This success was attained despite the factors previously mentioned as increasing the degree of risk in the patients, and it shows what may be accomplished by sound technic.

It therefore appears that the dangers attendant on total gastrectomy, both the possibility of anemia and the operative mortality, need not prove insurmountable. The control of anemia in the patients surviving the operation by the administration of extract of liver and the reduction

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3. Walters, W.: Total Gastrectomy, in Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935, pp. 628-635.

4. Allen, A. W.: Carcinoma of the Stomach, with Special Reference to Total Gastrectomy, Tr. South. S. A. **50**:165-175, 1937.

in the operative mortality by improvements already evident in the technic of the operation may permit indications for total gastrectomy accepted at present to be changed so that the operation will be performed in many cases of less than total and even only moderately extensive tumorous invasion of the stomach.

Before total gastrectomy can be justified as an acceptable clinical procedure, however, there must first be some basis for the belief that a better end result of total gastrectomy counterbalances the lower operative mortality rate of subtotal gastrectomy. Obviously, this cannot be proved from the figures now available, although the increase of radical operative procedures for malignant disease in other parts of the body has always improved the end results, and it seems reasonable to expect that operations on the stomach should be no exception. Many patients have lived longer after subtotal gastrectomy than any patient has lived after total gastrectomy. But no reported total gastrectomy has been attempted on a patient with less than practically total invasion of the stomach by tumor with the consequent probability of extension of the tumor beyond the limits of even total gastrectomy. In other words, in all instances of total gastrectomy for malignant disease of the stomach reported so far there has been little if any hope of cure, and the operations should be considered to have been essentially palliative procedures.

It was in an attempt to determine the end result of total gastrectomy and the chance of cure for patients with less than total invasion of the stomach by carcinoma that total gastrectomy was performed in 2 of the 4 personal cases reported hereinafter (cases 2 and 3).

The technic of the operation employed in the last 3 cases, in all of which the patients survived and were living and well at the time of writing, was evolved by the study of various technics employed in other recorded cases and by lessons learned through previous experience with subtotal gastrectomy and with total gastrectomy in case 1. No claim of originality is made. The postoperative convalescence of the last 3 patients suggests that the technic is sound.

THE OPERATION

Careful preoperative treatment, scrupulous operative technic and accurate postoperative treatment are all essential. Because a detailed account of the operation will be made the subject of another report, only a brief description will be given here.

Spinal anesthesia is believed to be most important in facilitating the operation. The technic employs anesthesia which usually persists for three or four hours. An upper midline incision is used. Total gastrectomy is accomplished by first completely mobilizing the entire stomach,

next severing the first portion of the duodenum, then gradually severing the lower end of the esophagus during the course of an anastomosis with the side of the first portion of the jejunum, which has been previously brought up through the transverse mesocolon. Because of the relation established between the jejunum and the mesocolon, enteroanastomosis does not seem necessary and is not used. Jejunostomy may be done, but it was not used in the cases hereinafter reported.

Aspiration at the site of gastrojejunostomy through a small nasal tube placed at the time of operation is constantly maintained for several days. Fluid balance is maintained by fluids and blood administered intravenously. Small amounts of fluids followed later by soft foods are given in eight or ten days, and within two weeks the patient readily tolerates a five meal type of diet. The meals must remain small for a time, but the jejunum eventually dilates so that regular meals are taken comfortably. Vitamins and possibly extract of liver should be given temporarily.

REPORT OF CASES

CASE 1.—W. C. G., a white man aged 55 years, was admitted to the University of Virginia Hospital Aug. 4, 1934. For eighteen months he had suffered with epigastric symptoms suggestive of duodenal or gastric ulcer or gastric carcinoma. During the last seven months he had lost 30 pounds (13.6 Kg.), and during the two weeks before admission his symptoms had become much more marked.

Physical examination revealed a palpable mass in the epigastrium, estimated at 4 cm. in diameter. Roentgen examination revealed carcinoma involving the lower two thirds of the stomach and an absence of six hour retention.

An operation was performed August 9. Spinal anesthesia induced with procaine hydrochloride, later supplemented with ether inhalation anesthesia, was employed. The operation lasted two hours and thirty minutes. An incision through the upper part of the right rectus muscle was made. Practically the entire stomach showed invasion by carcinoma, but no spread to adjacent structures or metastasis was evident. Total gastrectomy seemed necessary and feasible, and it was done. A postcolic esophagojejunal anastomosis was made, the technic of which varied from that employed in the other cases in several details now recognized as important. Nevertheless, the patient stood the operation well and was returned to his ward in excellent condition. The pathologic diagnosis was colloid carcinoma of the stomach without metastasis to the regional lymph nodes.

The postoperative convalescence was complicated by signs of pneumonic consolidation in the base of the left lung twenty-four hours after operation. The patient died of pneumonia four days after the operation. Necropsy confirmed pneumonia as the cause of death, for the peritoneum showed no more reaction than was to be expected after any gastric operation.

CASE 2.—L. L., a married white woman aged 48 years, entered the University of Virginia Hospital Jan. 8, 1939. During the preceding two years she had suffered periodically with symptoms typical of duodenal ulcer and had lost 35 pounds (15.9 Kg.). She had been under investigation and medical care in the outpatient department since Nov. 11, 1938. Roentgen examination of the stomach

had revealed a large gastric ulcer at the incisura angularis (fig. 1 *A*). Against advice, she deferred operation.

When she finally did enter the hospital, preparations for the operation were carefully carried out. On January 11, the operation was performed. Carcinoma affected only the lesser curvature of the stomach, though it involved that fairly extensively. There was no evidence of spread or metastasis of the tumor; and although extensive subtotal gastrectomy might have eradicated all grossly demonstrable tumor, it seemed to me that total gastrectomy offered a better prognosis. Therefore, the entire stomach was removed, according to the technic described previously. The operation occupied two hours and thirty minutes. The pathologic diagnosis was adenocarcinoma of the stomach with many features of colloid carcinoma. The lymph nodes were not involved.

The patient's postoperative convalescence was remarkably smooth, and her highest temperature was 100.4 F. by rectum. The nasal tube was removed nine days after operation. Fluids were being taken by mouth twelve days after operation, and soft foods were permitted two days later. She was discharged to her

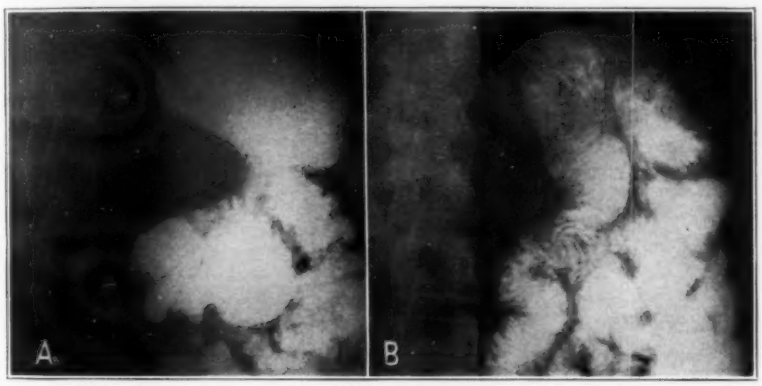

Fig. 1 (case 2).—*A*, carcinoma of the stomach; *B*, esophagojejunal anastomosis and reservoir-like dilatation of the afferent and efferent loops of the jejunum eleven weeks after total gastrectomy.

home on the seventeenth day after the operation, able to get about freely and tolerating a five meal diet.

Her course has been followed for over two years since the operation at intervals of from six weeks to three months. Her most recent visit was April 10, 1941. As early as March 28, 1939, eleven weeks after the operation, roentgen examination revealed a perfectly functioning esophagojejunal stoma with the formation of a reservoir for food as a consequence of dilatation of both the afferent and the efferent loops (fig. 1 *B*). She has continued to have an excellent appetite and, except for an occasional burning sensation in the throat relieved by taking a pinch of bicarbonate of soda, she has had no discomfort or other symptoms of abnormality. On Nov. 2, 1939, she stated that she had enjoyed a lunch consisting of a bowl of soup, a plate of lima beans, two glasses of water and a large slice of custard pie. The same day, analysis of 24 cc. of material aspirated from the jejunal reservoir revealed no hydrochloric acid and total acids of only 10 degrees.

Since the operation her weight has never returned to her original maximum though, except for minor fluctuations, it has been maintained at a constant level, about 15 pounds (6.8 Kg.) below her preoperative weight.

Careful study of her blood at frequent intervals has failed to demonstrate any important change. The hemoglobin content has not fallen below 70 per cent (Dare), and the lowest erythrocyte count has been 3,760,000. At that time, six months after operation, she was given some extract of liver and iron for a short time but has had no medication since then. At the time of her visit, Oct. 10, 1940, the hemoglobin was 80 per cent (Dare), and her erythrocyte count was 4,090,000. At the time of writing, more than two years after total gastrectomy, she appears to be well, healthy and free from any signs of recurrence or metastasis.

CASE 3.—A. S., a white man aged 38 years, entered the University of Virginia Hospital on Feb. 22, 1940, complaining of gastric symptoms of fourteen years' duration. Aggravation of the pain, nausea and vomiting had been troublesome during the last five months. In 1935 he had undergone an emergency operation

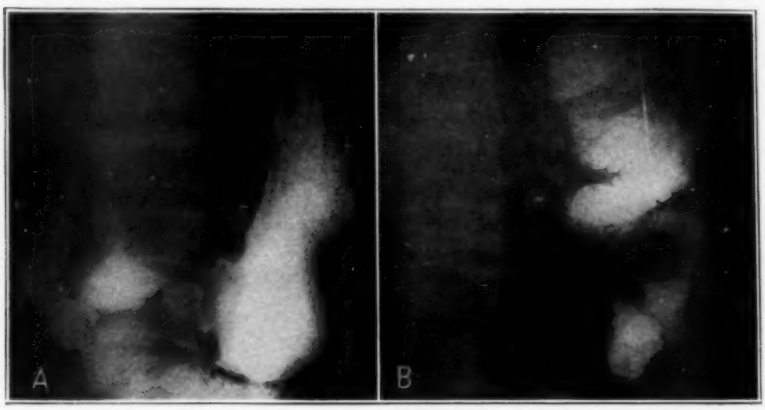

Fig. 2 (case 3).—*A*, carcinoma of the stomach; *B*, esophagojejunal anastomosis and reservoir-like dilatation of the afferent and efferent loops of the jejunum nine weeks after total gastrectomy.

elsewhere for simple closure of a perforated stomach ulcer. In 1937, again elsewhere, a posterior gastroenterostomy had been made. My investigation began in the medical outpatient department Feb. 14, 1940.

Except for sexual underdevelopment and evident loss of weight (20 pounds [9.1 Kg.]), physical examination showed him to be essentially normal. Roentgen examination of the stomach, however, revealed a functioning gastroenterostomy stoma and infiltration suggesting carcinoma in the lower half of the stomach (fig. 2 *A*).

The patient was carefully prepared for operation. On February 29 the operation was performed. Carcinoma involved practically the entire lower third of the stomach, but there was no sign of spread of the tumor or of metastasis. Total gastrectomy was decided on because of the relative youth of the patient (implying a poor prognosis) and the distortion of the stomach due to gastroenterostomy.

The jejunum was freed from the stomach, and the stoma in the jejunum was closed by suture. Total gastrectomy was performed according to the technic

already described, the esophagojejunal anastomosis being placed distal to the closed gastroenteric stoma in the jejunum. The operation consumed three hours, but the patient withstood it without difficulty. The pathologic diagnosis was colloid carcinoma of the stomach without involvement of the lymph nodes.

The patient's postoperative convalescence was entirely smooth; the highest temperature was 101 F. by rectum. The tube to the site of anastomosis in the esophagus was removed ten days after operation. Liquids were given by mouth the next day, and soft foods were allowed thirteen days after operation. He was discharged to his home on the seventeenth day after operation and tolerated a five meal diet without trouble.

His course since operation has been followed at regular intervals of six weeks and has been most satisfactory. He has had no complaint at any time except slight burning sensation in the throat controlled readily by taking a pinch of bicarbonate of soda. A good appetite and the ability to eat normal meals have been constant. Roentgen examination on May 2, two months after operation, revealed excellent function of the anastomosis and the formation of a reservoir for food by dilatation of both afferent and efferent loops (fig. 2 *B*). His weight rapidly increased to above his normal level and has been maintained. No anemia has been evident, but he has been given small amounts of extract of liver periodically. The last examination of the blood revealed a hemoglobin content of 80 per cent (Dare), and the erythrocytes numbered 4,300,000. On April 3, 1941, over one year after total gastrectomy, he was apparently well and healthy and showed no signs of recurrence or metastasis.

CASE 4.—S. A. C., a white man aged 61 years, entered the University of Virginia Hospital on Feb. 21, 1941, complaining of indigestion and pain in the epigastrium: The symptoms had started about a year before and at first had been intermittent. For the last two months, however, they had been almost constant, and he had vomited fairly frequently. Weight lost had amounted to about 30 pounds (13.6 Kg.).

Physical examination showed him to be essentially normal except for some enlargement of the prostate. Roentgen examination revealed a sclerosing carcinoma of the body of the stomach similar to linitis plastica. Only small areas of the stomach immediately adjacent to the pylorus and the esophagus seemed uninvaded.

After careful preoperative treatment for three days the patient was operated on February 25. The findings at operation confirmed the roentgen observations. Except for small cuffs of uninvaded tissue at the pylorus and the cardia, the entire stomach was like a tube of carcinoma. However, there was no sign of spread of the carcinoma beyond the stomach. Obviously, total gastrectomy was the only possible means of eradicating the grossly evident tumor.

Total gastrectomy was accomplished by the technic already described. The operation lasted two and a half hours. The pathologic diagnosis was diffuse carcinoma of the stomach, grade 4, with direct extension to the gastrohepatic and the gastrocolic omentum. The patient withstood the procedure well and had an entirely smooth and uneventful convalescence as far as the abdomen was concerned, though intercurrent prostatism necessitated the use of an indwelling catheter until the patient was allowed to get out of bed. The nasal tube was removed seven days after operation; the giving of liquids by mouth was started nine days after operation, and a day later soft foods were allowed. He was permitted to get out of bed on the twelfth postoperative day; a five meal diet was begun on the thirteenth day, and he went home on March 13, the sixteenth day, apparently in excellent condition. As in the other cases, plans have been made for follow-up examination at regular intervals. His condition was satisfactory at the time of his first follow-up visit on March 27.

SUMMARY AND CONCLUSIONS

At present total gastrectomy is performed on only a limited number of patients, only those with carcinomatous involvement of practically the entire stomach. In such cases the prognosis is practically hopeless, so that the operation must be regarded as having been only a palliative procedure. Consequently, most patients surviving the operation itself have died within a few months of recurrent or metastatic tumor, and no opportunity has been afforded for studying the end results of total gastrectomy from the standpoint of either remote physiologic effects or possible superiority over subtotal gastrectomy as a means of cure.

Because the end results of subtotal gastrectomy, even in the hands of the most experienced gastric surgeon, leave much to be desired and because recent developments in the technic of total gastrectomy appear to indicate the means of appreciably reducing the previously high mortality of patients subjected to the operation, it is suggested that the time may be ripe to attempt a real evaluation of total gastrectomy. A determination of the remote physiologic effects and the real end results in comparison with those of subtotal gastrectomy can be made only by performing total gastrectomy on patients with moderate tumorous invasion of the stomach and hence with a fair prospect of complete eradication of the tumor by surgical intervention. It seems reasonable to believe that the operative mortality can be lowered and that the end results will be improved to a point that may justify the use of total gastrectomy in many more cases than it is at present employed.

A technic for total gastrectomy has been described. The cases of 4 patients subjected to operation have been reported. In the first case the patient was not operated on by the described technic, and for this or some other reason he died of pnuemonia early in the course of his convalescence. The other 3 patients had a most uneventful and smooth convalescence and at the time of writing are still alive and well—one, over two years after operation; another, over one year after operation, and the last, a few weeks after leaving the hospital. The patients in cases 2 and 3 had only moderately extensive carcinoma of the stomach and would ordinarily have been treated by subtotal gastrectomy. They were subjected to total gastrectomy in an attempt to begin an evaluation of the end results of total gastrectomy on patients for whom more radical surgical treatment might offer a better outlook for cure.

ASEPTIC NECROSIS AND BONE DRILLING

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AND
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Bone drilling as a therapeutic procedure is not altogether modern. About a hundred years ago Daniel Brainard,[1] a professor of surgery in Chicago, experimented successfully with subcutaneous bone drilling in animals. This led him to employ it in treating pseudarthrosis in human beings. Brainard recorded his investigations in an elaborate study which he dedicated to no less a person than the chief surgeon of Napoleon, Larrey, who had assisted him with material and experience. In Ollier's comprehensive book,[2] bone drilling is plainly referred to as "méthode Brainard." For all this, the procedure lapsed into oblivion.

About ten years ago the method was rediscovered and during the last decade has become a recognized means of treating delayed formation of callus and certain forms of pseudarthrosis. It seems obvious now that bone drilling with the consequent freshening of the bone, the formation of hematoma and the production of small detached and necrotic particles of bone should stimulate the formation of new bone.

Equally well conceived and borne out by practical results is the procedure of drilling in cases of slipping of the upper epiphysis of the femur. It brings about premature ossification of the epiphysial disk and thus prevents further progress of the deformity.

Treatment by bone drilling, however, has been extended to other conditions in which the theoretic foundation is less clear, for instance, to osteoarthritis. Yet, as a matter of fact, we have had occasion to observe that there is a distinct decrease of pain for some time after drilling of arthritic hip joints.

Finally, this form of treatment has been recommended for Perthes' disease and other forms of aseptic bone necrosis.[3] It is particularly

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From the Orthopedic Service of Bellevue Hospital.

Read at the Ninth Annual Convention of the American Academy of Orthopedic Surgeons, New Orleans, Jan. 14, 1941.

1. Brainard, D.: Mémoire sur le traitement des fractures non réunies et des difformités des os, Paris, J. B. Baillière, 1854.

2. Ollier, L.: Traité expérimental et clinique de la régénération des os et de la production artificielle du tissu osseux, Paris, V. Masson & fils, 1867.

3. Bozsan, E. J.: A New Treatment of Intracapsular Fractures of Neck of Femur and Calvé—Legg-Perthes' Disease, J. Bone & Joint Surg. **14**:884, 1932; **16**:75, 1934.

difficult to judge the influence of drilling on aseptic bone necrosis, for regardless of the type of treatment the subjective findings are usually insignificant, the healing time varies rather widely, and, above all, the stages of pathologic development seem to follow a definite course. It may be noted that the pathologic peculiarities of aseptic bone necrosis have not generally been given much emphasis. However, it is against

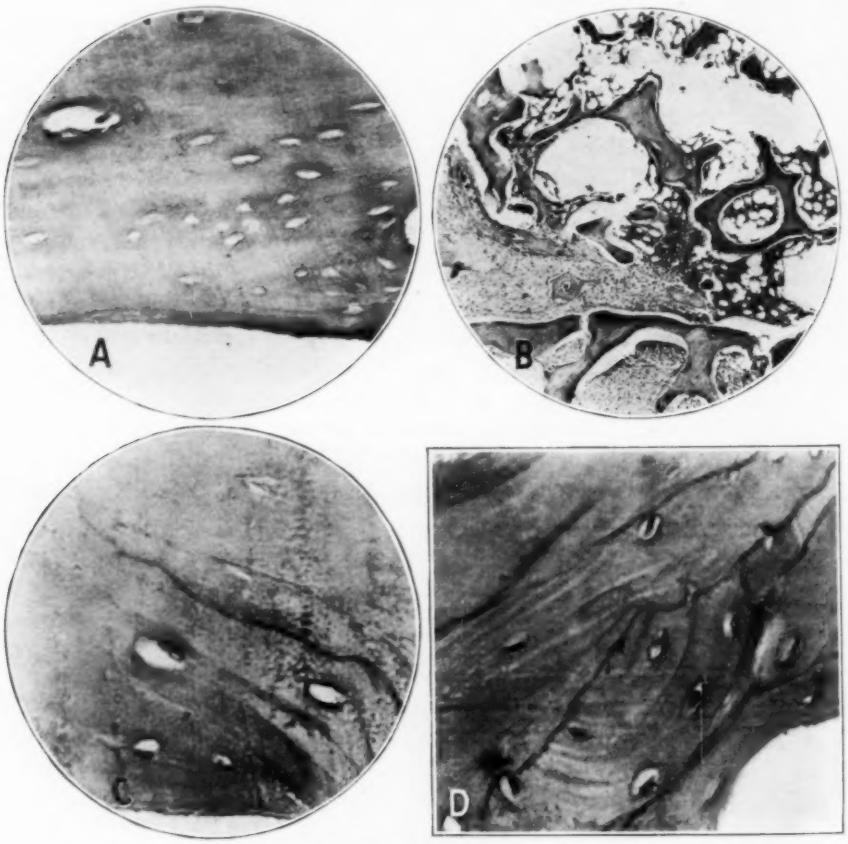

Fig. 1.—*A*, longitudinal section of a fibula of a dog two weeks after transplantation; the nuclei have disintegrated, leaving empty holes in the bony substance. *B*, lower third, invasion by fibrous tissue and blood vessels and formation of new bone; upper part, necrotic trabeculae and spaces filled with debris. *C*, newly built living bone demarcated from the dead lamella by a cement line. *D*, newly laid bone in an irregular arrangement (mosaic structure).

just this background that one must view the possible effect of drilling. The essential pathologic features will therefore be briefly reviewed.

It is only recently that physicians have come to know anything of this form of bone necrosis. Experimentation with bone transplants furnished

the initiative. Since Ollier's fundamental experiments, the superiority of autoplastic osteoperiosteal grafts over other forms of bone transplants has been established. The practical application of the findings in that experimentation was advanced particularly by the work of Albee. While Ollier and his contemporaries believed in the survival of the transplant,

Fig. 2.—*A*, normal upper femoral epiphysis of an adolescent rabbit. *B*, head of the femur of the adolescent rabbit about two months after circumcision of the capsule of the hip joint and severance of the ligamentum teres femoris; the epiphysial bone and marrow are necrotic; the bone trabeculae are pressed together, particularly in the subchondral region; the joint cartilage is alive and thickened because endochondral ossification is suspended. *C*, the head of a femur of another rabbit after the same time and procedure; invasion of the fibrous medulla is already present throughout the epiphysis; replacement of bone is under way, absorption prevailing; the epiphysis is flattened.

Barth [4] was able to demonstrate that bone grafts could turn necrotic and yet heal in. Barth's findings were in large part proved correct and, in the last analysis, were the foundation on which rested subsequent

4. Barth, A.: Ueber Osteoplastik, Arch. f. klin. Chir. **86**:859, 1908.

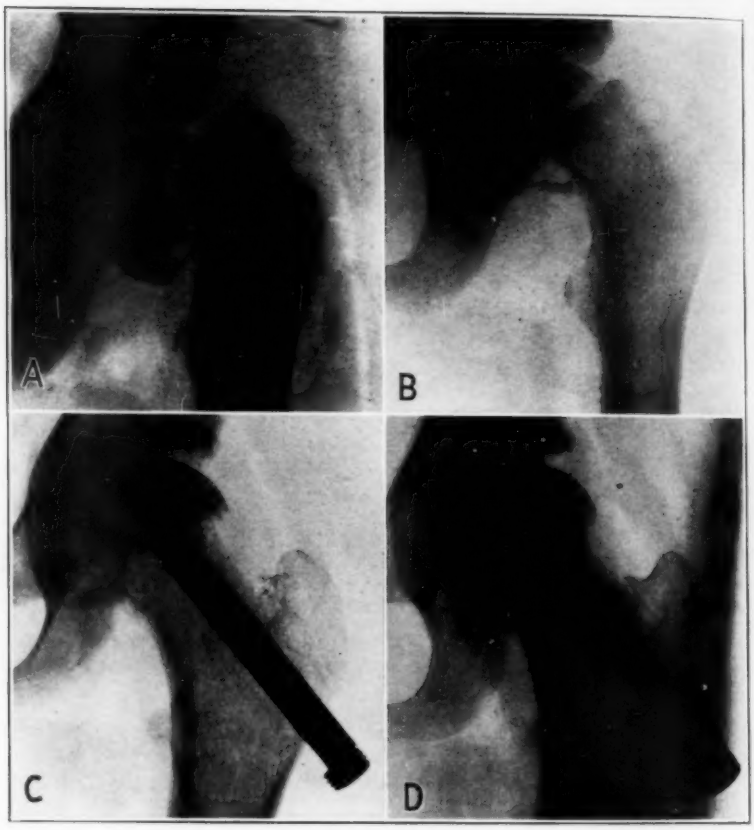

Fig. 3.—The correlation of the pathologic state of a bone with the roentgen observations is illustrated in this figure and in figure 4. *A*, recent epiphysial separation in a 12 year old girl. Roentgenologically it cannot as yet be said whether there is necrosis of the head of the femur. *B* shows that after traction for three weeks the head has retained its original density and that the shaft is markedly decalcified as a result of disuse; the same disuse has failed to produce any changes in the head, and it may therefore be assumed that circulation to the head is interrupted. *C* shows that the closed reduction has been completed and that subsequent nailing has been done to maintain proper alinement; the contrast in density is pronounced. *D*, taken three months after nailing, indicates that function has been resumed and that the density of the shaft has come back to normal; on the other hand, the head has begun to lose some of its density, and this implies that restitution is on its way; at the same time, it may be seen that necrosis of the head does not necessarily interfere with bone union.

investigations by Axhausen,[5] Phemister [6] and others, who showed the important role played by aseptic necrosis in bone disease apart from that due to transplantation.

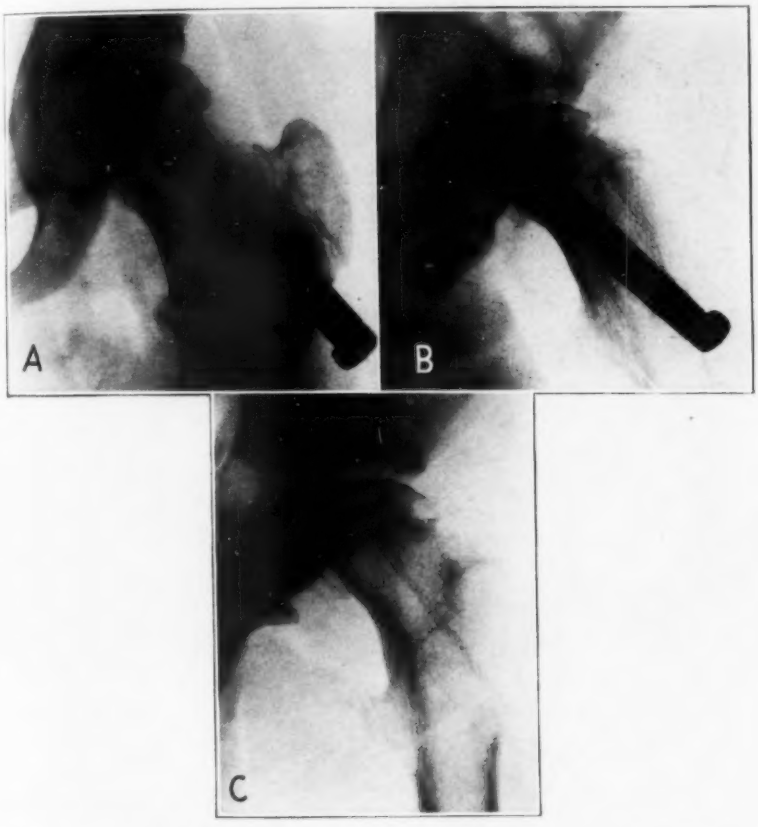

Fig. 4.—*A*, taken six months after operation, shows that the density and the structure of the head also have returned to normal; the process of healing seems to be finished. *B*, taken a year after nailing, shows that pathologic fracture and collapse of the head of the femur have occurred, apparently before bony substitution was completed. *C* shows that the nail, no longer serving a useful purpose, has been removed. The picture, if one did not know the history, would suggest Perthes' disease in the stage of fragmentation and condensation.

5. Axhausen, G.: Die histologischen und klinischen Gesetze der freien Osteoplastik auf Grund von Thierversuchen, Arch. f. klin. Chir. **88**:23, 1908. Axhausen, G., and Bergmann, E.: Die Ernährungsunterbrechungen am Knochen, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1937, vol. 9, pt. 3.

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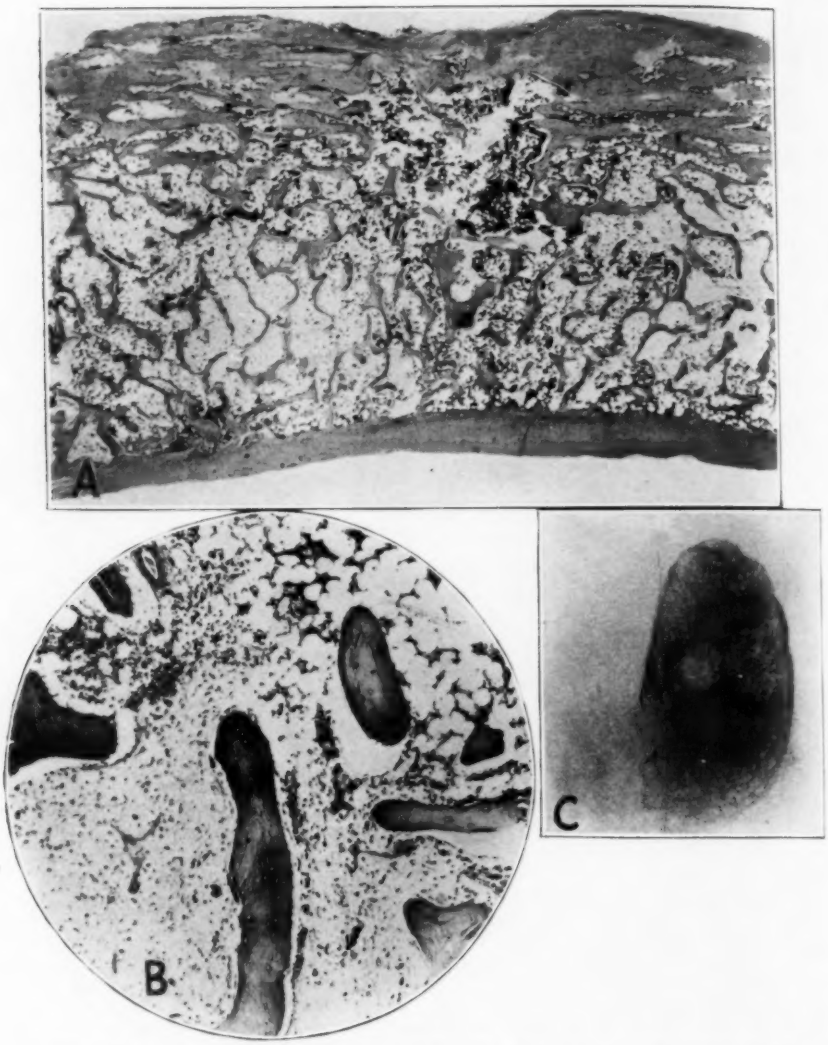

Fig. 5.—*A*, photomicrograph of a patella of a dog two months after drilling; the beginning of fibrous invasion is shown in the lower left corner. *B*, photomicrograph of a higher magnification of the invaded region far away from the drill canal, showing capillaries and connective fibers pushing forward toward the dead medulla. *C*, roentgenogram showing that loss of density proceeds from the periphery and that the region of the drill hole has not yet been reached.

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6. Phemister, D. B.: Changes in Bones and Joints Resulting from Interruption of Circulation, Arch. Surg. **41**:436 (Aug.); 1455 (Dec.) 1940; Repair of Bone in Presence of Aseptic Necrosis Resulting from Fractures, Transplantations, and Vascular Obstructions, J. Bone & Joint Surg. **12**:769, 1930; Aseptische Knochennekrose bei Fracturen, Transplantationen und Gefässverschlüssen, Ztschr. f. orthop. Chir. **55**:161, 1931; Fractures of Neck of Femur, Dislocations of Hip, and Obscure Vascular Disturbances Producing Aseptic Necrosis of Head of Femur, Surg., Gynec. & Obst. **59**:415, 1934.

Information about the vital processes of bone can be ascertained only from microscopic sections. Roentgen and gross appearances, valuable though they may be, are subject to interpretation. To gross inspection, dry and crumbling marrow is indicative of necrosis of the surrounding

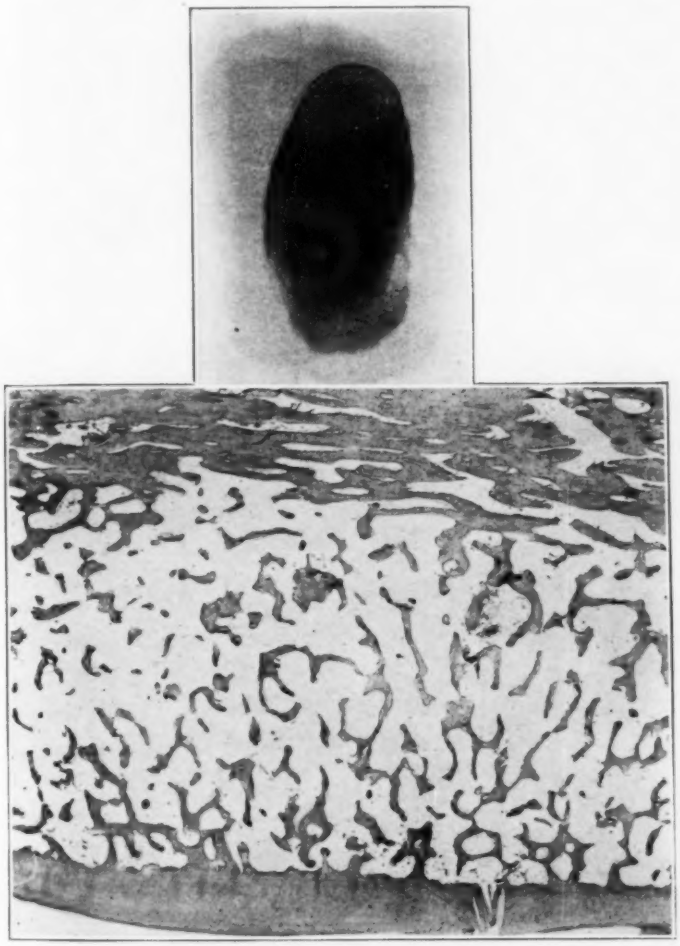

Fig. 6.—Roentgenogram and photomicrograph of the other (undrilled) patella of the dog in figure 5, showing that reorganization has not yet begun on this side; there is moderate production of bone at the lower end of the patella, apparently starting from surviving periosteum.

bone; in the roentgenogram the dead bone usually retains its original density in contrast to the adjacent living bone, which sooner or later shows signs of atrophy. Even microscopic observations, in view of the physical properties of bone tissue, require cautious evaluation.

Characteristic of bone necrosis is the failure of the nuclei to stain. However, interruption of the blood supply is not immediately followed by noticeable changes. At the end of the first week the nuclei may not be visibly impaired. This indifferent stage is followed by another stage

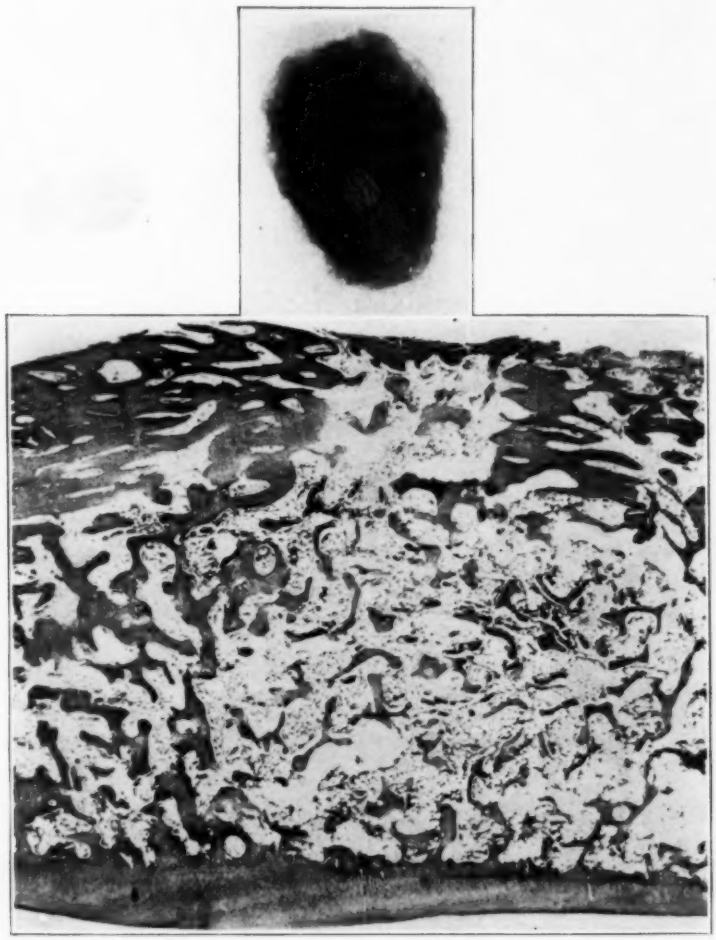

Fig. 7.—Roentgenogram and photomicrograph of the drilled patella of the dog in figures 5 and 6 after three months. As far as the process of repair is concerned, there is practically no difference between this and the undrilled side, shown in figure 8. In both this and the undrilled patella atrophy began at the periphery. There were no changes of density or structure around the drill canal.

in which pyknosis occurs. The cells may remain in this stage for some time. In the center of the necrotic areas, shrunken deeply stained nuclei may be observed for many months. However, this should not lead one

to believe that the bone has in part survived; this mistake is met with here and there in the literature. Then follows a third stage in which the nuclei disintegrate, leaving empty spaces in the bony substance which indicate their former places. Cells of the periosteum and the medulla

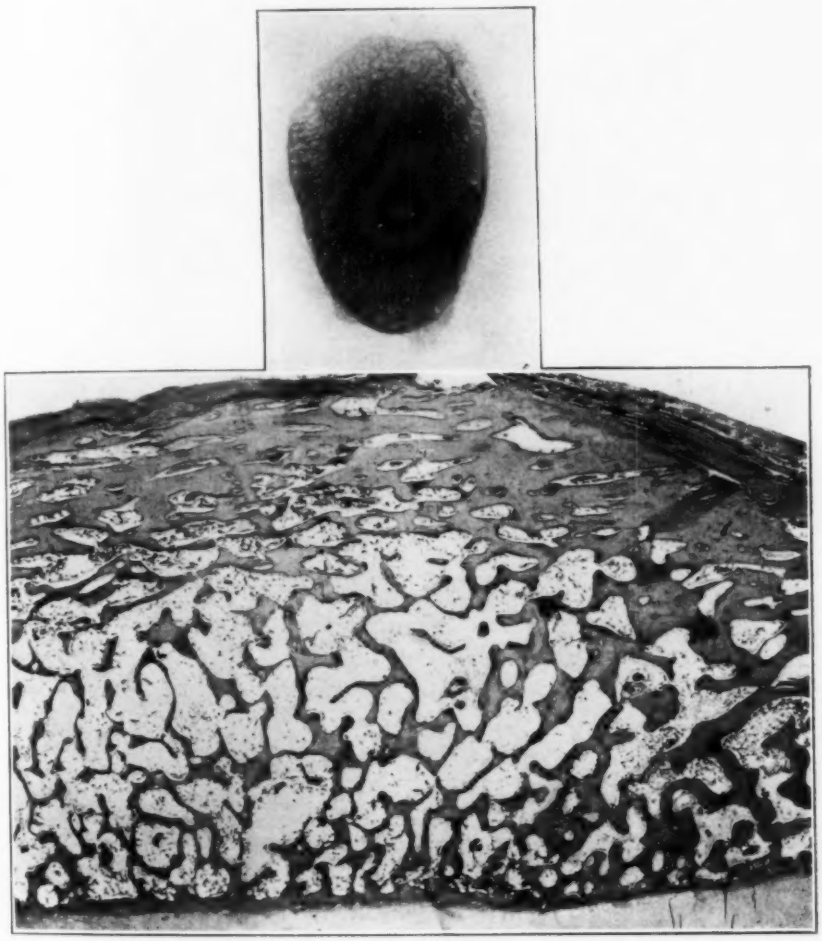

Fig. 8.—Roentgenogram and photomicrograph of the undrilled patella of the dog in figures 5, 6 and 7 after three months. From the roentgenogram it is evident that the bone has still retained more of its original density, indicating the slowness of restitution; this may have been due to the large size and the thickness of these knee caps. Apparently the undrilled side was the farther progressed.

seem less sensitive to the lack of blood supply, although in cases of epiphysial necrosis the marrow, in part or in whole, is dead. The joint cartilage, deriving its nutrition mainly from the synovial fluid, may or may not show signs of impairment.

Now, in contrast to what happens in osteomyelitic sequestration, in aseptic necrosis a process of restitution soon sets in with the ultimate objective of replacing the dead with new bone. To this end, capillaries and connective fibers originating from adjacent living marrow and

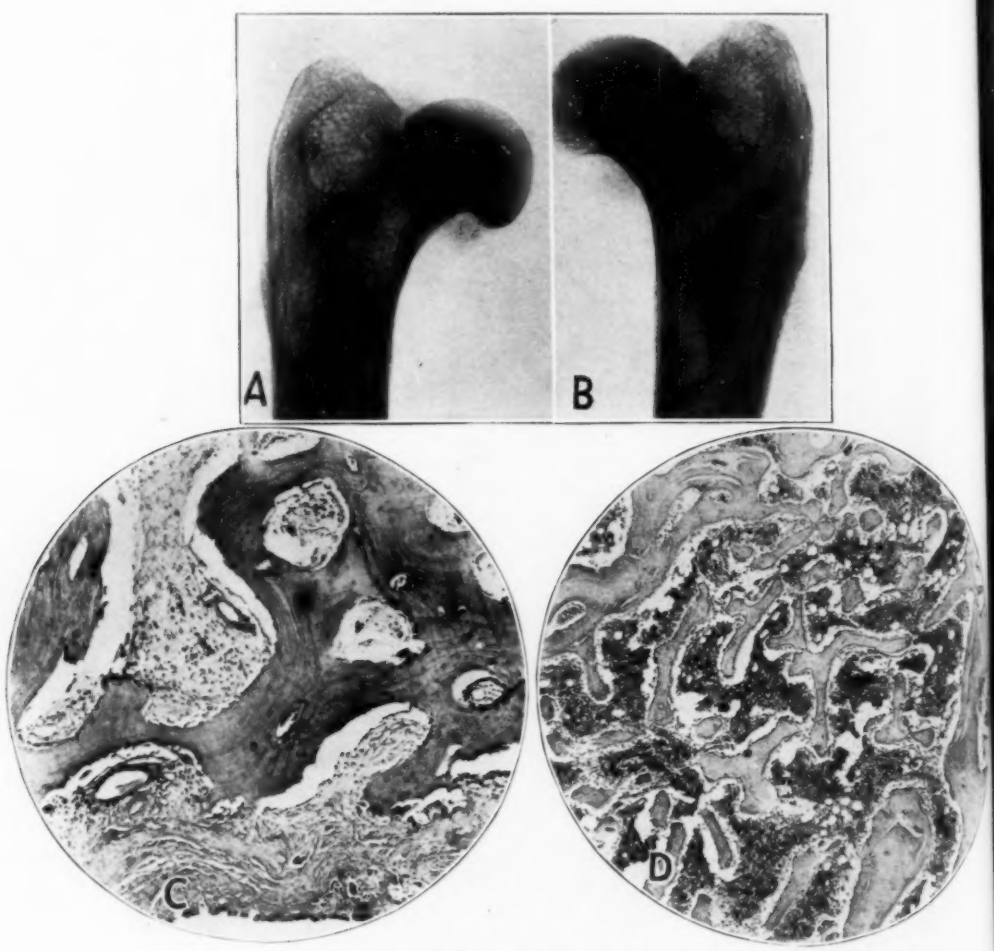

Fig. 9.—*A*, roentgenogram of the undrilled head of a femur of a dog two months after operation; the changes in density are more outspoken on this side. *B*, roentgenogram of the drilled head of the other femur; there is no indication of atrophy starting around the drill canal. *C*, photomicrograph of a section of the undrilled head; invasion by the vessels and the connective fibers starts from the periosteal cover of the neck of the femur, where it meets the joint cartilage. *D*, photomicrograph of a section of the drilled head; fragments of dead substantia spongiosa may be seen within the drill canal; the spaces are filled with debris from dead marrow cells and disintegrated blood.

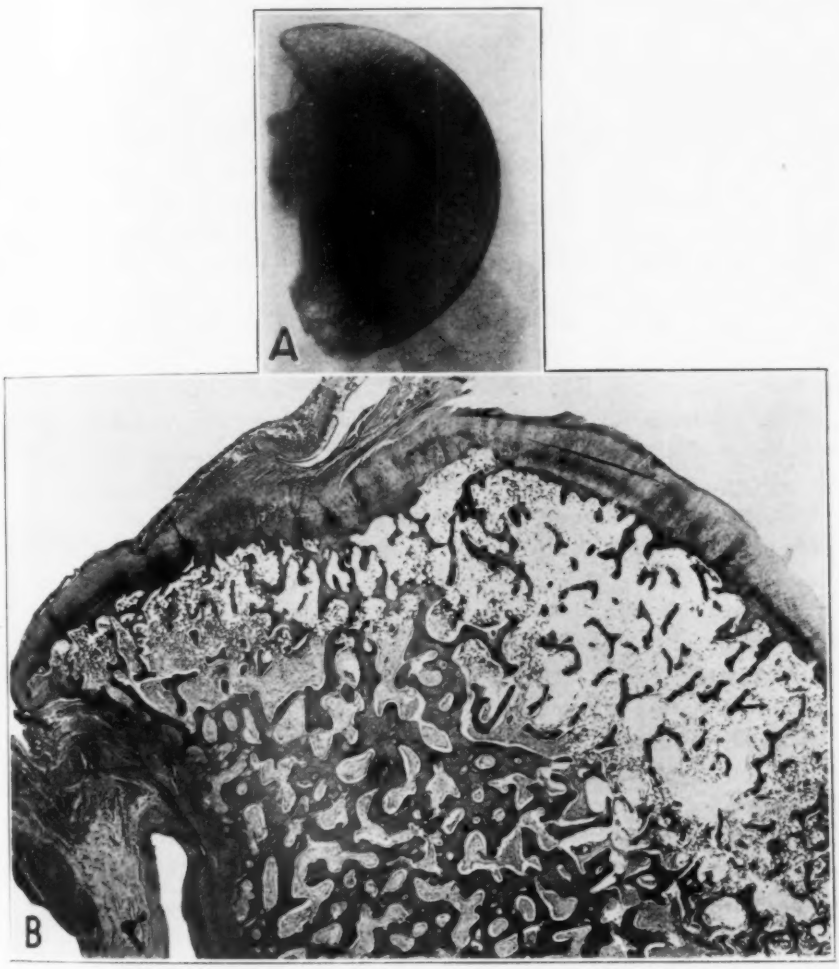

Fig. 10.—*A*, roentgenogram of the head of a femur of a dog eight months after intracapsular fracture and drilling, showing that the subchondral necrotic area is less dense than normal, while the region of bony replacement is condensed beyond normal owing to an increase in the number and the size of bone trabeculae with consequent reduction of the spaces in the medulla. *B*, photomicrograph of the same head. The fracture ended in fibrous union. About two thirds of the head had undergone reorganization. In this area the bone trabeculae were increased in number and size by the lively deposition of new bone. Abruptly beyond this regenerated area was a zone of complete necrosis of bone and marrow. The sharp contrast between the finished regeneration of the greater part of the head and the total necrosis of the rest, together with the absence of any zone of transition, may illustrate the arrest of revitalization described by Phemister.

periosteum start to invade the spaces of dead substantia spongiosa. This fibrous tissue may contain giant cells in considerable number. Normally, fibrous invasion soon spreads over the entire area of necrosis. There is reason to emphasize that at this stage the bone trabeculae are still dead. If such a revascularized area of necrosis is cut through, it will bleed, giving the erroneous impression that the bone is alive. In fact, this has misled Ollier and many others.

The next phase is characterized by the replacement of the bone tissue proper. The invading connective fibers, because of their origin, carry specific components for bone formation and absorption. As a rule, resorption outweighs temporarily the deposition of new bone. Hence, the roentgen picture changes from the original density to atrophy and less distinct structure.

Elimination of dead bone is brought about either by lacunar resorption (that is, through the activity of specific cells, osteoclasts) or by way of creeping substitution. In the latter process, the new bone itself is thought to dissolve the necrotic one. Creeping replacement, long a matter of dispute, is still poorly understood in its exact details.

In general, newly formed bone is sharply demarcated from the old by a cement line. Also regarded as characteristic of new bone is its mosaic structure, in other words, the irregular arrangement of its lamellas. Later the structure adjusts itself to the requirements of function.

The normal course of restoration thus far outlined could be completed within several months if undisturbed. Usually, however, there are disturbances which greatly delay the process of repair. The dead epiphysis, since it is less resistant, may crumble through physical stress, form pathologic fractures and collapse; this condition is present when roentgen examination reveals fragmentation and condensation. The small fragments, pressed by weight bearing into a solid mass of bone sand, may form a barrier against the invading tissue and cause retardation of the revitalizing process. The course of restoration may even be entirely interrupted at any stage, as it is in cases of osteochondritis dissecans. As in this condition, so in cases of fracture of the neck of the femur a wedge-shaped piece of dead bone may separate from the upper quadrant of the head of the femur; however, this does not occur until the fracture has healed, for apparently only then do the mechanics of weight bearing come fully into play. Strangely, this separation may occur after two years or more, at a time, therefore, when all necrotic bone should long since have been replaced. This seems to indicate that the capacity of repair may be exhausted before attaining its aim, particularly in old age, as Phemister has pointed out.

It would be logical to expect the separation to take place at a line of demarcation between a living and a dead zone. In fact, however, it usually occurs within the dead area. Incidentally, this occurs also in cases of osteomyelitis, in which the sequestrum is often only part of the necrosis.

Such in short is bone disease as it ensues from interruption of blood supply under aseptic conditions. Obviously, the different phases of reorganization follow rather definite rules. It is hard to conceive that drilling should bring about a fundamental change, though it may speed up the natural course.

To arrive at a more precise understanding of the effect of drilling it seemed worth while to check on this question by experimentation. In earlier experiments one of us (E. B.) [7] had produced aseptic bone necrosis by circumcision of the joint capsule of the hip and simultaneous severance of the ligamentum teres femoris. The necrosis corresponded in extent to that found in cases of intracapsular fracture of the neck of the femur. Another method of producing aseptic necrosis is to ligate all soft tissues about the patella. Experiments along these lines were resumed in the Laboratories of Experimental Surgery, of which Dr. Frank W. Co-Tui is director. The intent was to produce bilateral necrosis of the head of the femur or the patella and to drill one side and leave the other to its natural course. Fourteen animals, mostly grown-up dogs, were used, but because of death, infection or failure to show necrosis, 6 animals were eliminated.

The results of the experiments carried out with the 8 remaining animals may be summarized briefly as follows: Specimens were examined after two, three and eight months. Differences between the drilled and the undrilled side were but slight whether expressed in terms of microscopic or of roentgen observation. In 1 instance, though, revascularization was fairly advanced in the drilled bone, while the bone of the other side still remained almost inactive. However, fibrous invasion began some distance from the drill hole at a point where the periosteum and the joint cartilage met. In later stages no distinct signs were observed in the way of a more advanced restitution of one side. The revitalizing process proceeded mainly from the periosteum-covered surface. The drill canal and its immediate surroundings gave no conclusive evidence of initial fibrous invasion.

7. Bergmann, E.: Theoretisches, Klinisches und Experimentelles zur Frage der aseptische Knochennekrosen, Deutsche Ztschr. f. Chir. **206**:12, 1927; Der Anteil der einzelnen Wachstumzonen am Längenwachstum der Knochen, ibid. **213**:303, 1929; Osteochondritis dissecans des Hüftgelenks, ibid. **217**:400, 1929; Ueber das Längenwachstum der Knochen, ibid. **233**:149, 1931; Spätschäden nach geheilten Schenkelhalsbrüchen, ibid. **245**:496, 1935.

The nature of our experiments and observations call for cautious interpretation. It may be stated that drilling perhaps facilitates revascularization. However, we were unable to demonstrate changes significant enough to permit the recommendation of drilling as a useful therapeutic measure in cases of aseptic necrosis of bone.

Practical considerations make us hesitate to recommend drilling in cases of Perthes' disease, since it brings about premature closure of the epiphysis. This fact is of less significance in cases of slipping of the epiphysis because this condition occurs in adolescents. In cases of Perthes' disease, a condition which occurs between the ages of 5 and 9 years, drilling is more likely to cause shortening.

INCONSTANT SYMPATHETIC NEURAL PATHWAYS

THEIR RELATION TO SYMPATHETIC DENERVATION OF THE UPPER EXTREMITY

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The sympathetic innervation of the upper extremity is derived mainly from the cervicothoracic and middle cervical sympathetic trunk ganglions via gray communicating rami which join the lower cervical nerves from the fifth to the eighth and the first thoracic nerve. The inconstant intrathoracic ramus of the second thoracic nerve which joins the first conveys sympathetic fibers arising in the second thoracic and possibly lower ganglions of the sympathetic trunk into the brachial plexus (Kuntz).[1] In consequence of this finding, operative procedures for the sympathetic denervation of the upper extremity have generally been modified to include extirpation of the second thoracic segment of the sympathetic trunk, with the inferior cervical and first thoracic segments. This operation, as usually carried out, interrupts all generally recognized sympathetic pathways into the upper extremity. In some instances it fails to effect complete functional sympathetic denervation of the extremity. The persistence of functionally intact sympathetic fibers in the upper extremity in certain cases after extirpation of the inferior cervical and first and second thoracic segments of the sympathetic trunk suggests that there exist in these cases other pathways than those commonly recognized through which sympathetic nerve impulses reach the upper extremity.

The operative procedure, as usually carried out, does not include removal of the middle cervical ganglions, but all preganglionic fibers which reach these ganglions via the white communicating rami of the first thoracic or lower spinal nerves are interrupted. These ganglions are consequently functionally eliminated unless certain preganglionic fibers reach them via the lower cervical nerves. The existence of pathways outside the sympathetic trunk through which sympathetic fibers

From the St. Louis University School of Medicine.

1. Kuntz, A.: Distribution of the Sympathetic Rami to the Brachial Plexus: Its Relation to Sympathectomy Affecting the Upper Extremity, Arch. Surg. **15:** 871-877 (Dec.) 1927.

arising at levels lower than the second thoracic segment may reach the brachial plexus is not precluded. In 1931 Adson [2] advanced the opinion that some fibers which join the cardiac plexus via the thoracic cardiac nerves may traverse this plexus and reach the upper extremity. In 1941, by an experimental anatomic study carried out on cats, Van Buskirk [3] demonstrated that some of the fibers which enter the vertebral canal from sympathetic trunk ganglions at lower levels ascend in the sinuvertebral nerve and join the ventral roots of the lower cervical and first thoracic nerves, through which they may enter the upper extremity.

A contribution of sympathetic fibers to the upper extremity via the cardiac plexus has not been actually demonstrated. Those fibers which enter the upper extremity via recurrent rami from the nerves in the vertebral canal are probably not sufficiently numerous to account for the manifestation in certain cases of functionally intact sympathetic fibers in the extremity after sympathectomy. The present investigation has been undertaken to determine more accurately the sources of the sympathetic fibers which enter the upper extremity and the anatomic pathways through which they join the brachial plexus.

In pursuance of this investigation 44 cadavers, all of which were used in the dissecting room during the school year (1940-1941), have been examined. Complete dissections of the thoracic and cervical portions of both sympathetic trunks including their connections with the spinal nerves were carried out in every case. Early in this work, one of us (H. D. K.) discovered a ramus arising from the third thoracic nerve just distal to the junctions of the communicating rami with it and joining the second thoracic nerve at approximately the same distance from its communicating rami. The frequency with which this ramus is present was carefully noted. In some instances it was removed and prepared for microscopic study. Several of these rami obtained at autopsy also were prepared for microscopic study. Particular attention also has been given the connections of the eighth cervical nerve with the cervicothoracic and lower middle cervical ganglions, including microscopic study of the proximal communicating ramus of the eighth cervical nerve in some cases.

ANATOMIC DATA

The anatomic relations of the thoracic and cervical portions of the sympathetic trunks and the arrangement of the communicating rami in

2. Adson, A. W.: Cervicothoracic Ganglionectomy, Trunk Resection and Ramisectomy by the Posterior Intrathoracic Approach, Am. J. Surg. **11**:227-232, 1931.

3. Van Buskirk, C.: The Nerves in the Vertebral Canal and Their Relation to the Sympathetic Innervation of the Upper Extremities, Arch. Surg. **43**:427-432 (Sept.) 1941.

general conform to current textbook accounts. A discrete inferior cervical ganglion occurs only rarely. In most instances the inferior cervical and first thoracic ganglions are fused, giving rise to a cervicothoracic or stellate ganglion which is highly variable in size and form. This ganglion is commonly located in the interval between the eighth cervical and first thoracic nerves and is usually connected with the first thoracic nerve by two communicating rami, with the eighth cervical by two, with the seventh cervical by one and sometimes with the sixth cervical by one. A large ramus arising from the superior border of this ganglion and extending upward along the posterior aspect of the vertebral artery gives rise to branches which form the major portion of the plexus on this artery and to relatively small rami which join the seventh and sixth cervical nerves. The gray rami arising from the cervicothoracic ganglion which join the cervical and first thoracic nerves obviously include the major portion of the sympathetic fibers which enter the upper extremity.

According to current textbook accounts, the middle cervical ganglion is absent in a high percentage of cases. This statement evidently refers to the ganglion which, when present, is located about the level of the sixth cervical segment. A ganglion located approximately at this level was present bilaterally in 13 and unilaterally in 2 of the 44 cadavers examined. This ganglion has been designated by Axford [4] as the high type of middle cervical ganglion. It usually appears as a well defined enlargement on the cervical sympathetic trunk, from which communicating rami join the sixth and fifth and sometimes the fourth and seventh cervical nerves.

In all the cadavers examined there was present bilaterally another ganglion located on the medial side of the vertebral artery, approximately at the level of the eighth cervical nerve. It is relatively small in some cases but always clearly distinguishable (fig. 1). This ganglion has been designated by Axford as the low type of middle cervical ganglion. It is connected with the cervicothoracic ganglion by a large ramus which passes behind the vertebral artery and usually by another smaller one which passes in front of this artery. In most cases it is also connected with the cervicothoracic ganglion through the ansa subclavia. Few communicating rami arising from this ganglion join the brachial plexus. Frequently such a ramus joins the sixth cervical nerve, and rarely one joins the fifth or seventh. In cases in which there is a white communicating ramus associated with the eighth cervical nerve, some of its fibers may pass directly to the low middle cervical ganglion.

4. Axford, M.: Some Observations on the Cervical Sympathetic in Man, J. Anat. **62**:301-318, 1927.

The first sympathetic trunk ganglion below the cervicothoracic, i. e., the second thoracic ganglion, is located at the level of the second thoracic nerve. It is connected with this nerve by a white and a gray communicating ramus. This ganglion has a peculiarly significant relation to the sympathetic innervation of the upper extremity, since many fibers which join the second thoracic nerve through its gray communicating ramus traverse the intrathoracic ramus of this nerve, which

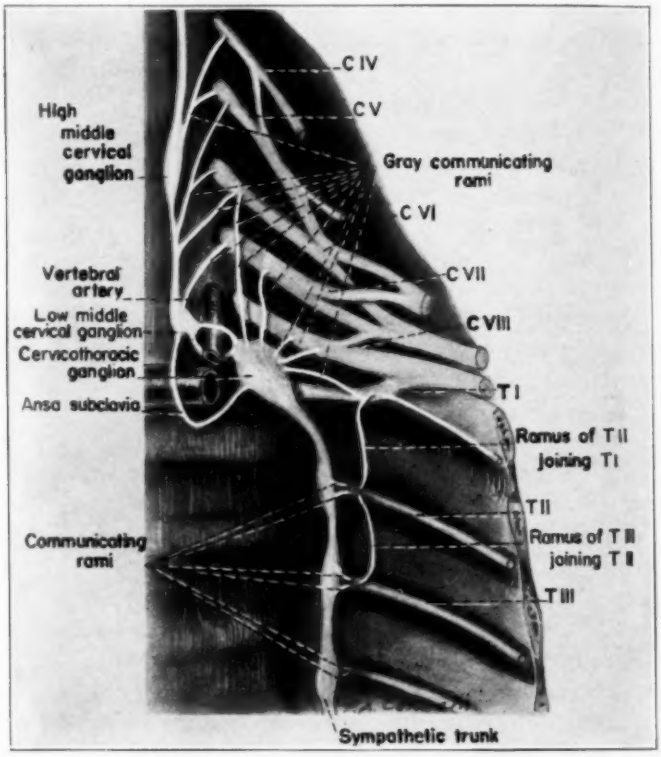

Fig. 1.—Drawing from a cadaver to illustrate anatomic relations of middle cervical, cervicothoracic and upper thoracic sympathetic trunk ganglions and rami from the second (*T II*) to the first thoracic nerve (*T I*) and from the third (*T III*) to the second thoracic nerve.

joins the first thoracic nerve, and enter the brachial plexus.[1] The intrathoracic ramus extending from the second to the first thoracic nerve was present bilaterally in 26 and unilaterally in 14 of the 44 cadavers examined. In the present series the percentage of cases in which this ramus could be demonstrated is somewhat higher than in the series studied earlier by Kuntz.

The second sympathetic trunk ganglion below the cervicothoracic, i. e., the third thoracic ganglion, is located at the level of the third thoracic nerve. It is connected with this nerve by a white and a gray communicating ramus.

A ramus arising from the third thoracic nerve just distal to the junctions of the communicating rami with this nerve and joining the second thoracic nerve (figs. 1 and 2) was demonstrated bilaterally in 15 and unilaterally in 18 of the 44 cadavers examined. In 6 of the remaining 11 cadavers, in which no direct communication between the third and second thoracic nerves could be demonstrated, a ramus arising from the third thoracic nerve either joined the second thoracic sympathetic ganglion or the sympathetic trunk just below this ganglion. In all cases in which the ramus arising from the third thoracic nerve joins the second, the junction occurs in proximity to the junction of the

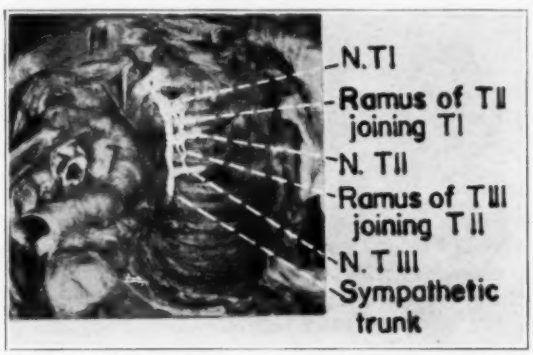

Fig. 2.—Photograph of a dissection showing the upper thoracic segments of the sympathetic trunk and rami from the second (*N. T II*) to the first thoracic nerve (*N. T I*) and from the third (*N. T III*) to the second thoracic nerve.

gray communicating ramus with the latter nerve or takes place directly with its gray communicating ramus and, consequently, in proximity to the origin of the ramus of the second thoracic nerve which joins the first. In some cases the ramus arising from the third thoracic nerve divides and joins the second at more than one point (fig. 2). In a few instances one branch could be traced directly into the ramus arising from the second thoracic nerve, which joins the first. The ramus in question, that arising from the third thoracic nerve, lies closely applied to the anterior surface of the third rib and the intercostal muscle and is embedded in the loose areolar connective tissue which lies in relation to the sympathetic trunk. If, instead of joining the second thoracic nerve, it joins the second thoracic sympathetic ganglion or the sympathetic trunk below the latter ganglion, it may be completely concealed by the connective tissue.

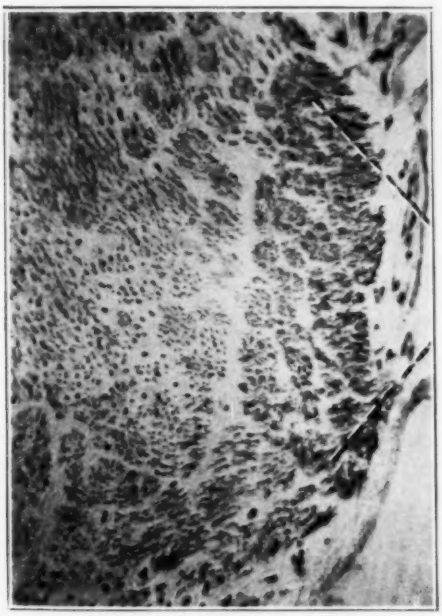

Fig. 3.—Photomicrograph of a transverse section of a ramus arising from the third thoracic nerve and joining the second. The broken lines indicate a peripheral area occupied by sympathetic fibers. Sympathetic fibers also are present in small groups among the somatic fibers.

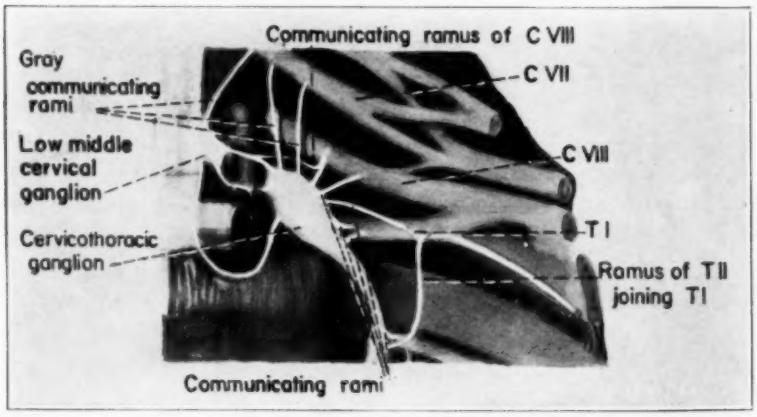

Fig. 4.—Drawing from a cadaver illustrating a communicating ramus of the eighth cervical nerve (*C VIII*) which joins both the cervicothoracic and the low middle cervical ganglions.

Microscopic study of transverse sections of the ramus extending from the third to the second thoracic nerve shows that the ramus includes unmyelinated fibers undoubtedly of sympathetic origin. Many of these are aggregated in a well defined bundle at the periphery of the ramus (fig. 3). Others occur in small groups of closely aggregated unmyelinated fibers between the larger myelinated somatic fibers. The percentage of sympathetic fibers in this ramus is greatly in excess of that normally present in the peripheral rami of the thoracic nerves.

In some cases one of the communicating rami which connects the cervicothoracic ganglion with the eighth cervical nerve bifurcates and sends one division into the low middle cervical ganglion (fig. 4). This ramus, as revealed by microscopic study of transverse sections, is made up mainly of unmyelinated fibers of small caliber which are undoubtedly postganglionic. In some instances small myelinated fibers are present among the unmyelinated ones. These myelinated fibers probably are mainly preganglionic fibers which in these cases emerge through the eighth cervical nerve. This communicating ramus, therefore, constitutes a pathway through which in certain cases some preganglionic fibers may reach the low cervical sympathetic ganglion without traversing the cervicothoracic ganglion.

CONCLUSIONS

The anatomic data set forth in the present paper show clearly that not all the sympathetic fibers which join the nerves of the brachial plexus (and which, consequently, may enter the upper extremity) traverse the gray communicating rami arising from the cervicothoracic and middle cervical ganglions. The intrathoracic ramus of the second thoracic nerve which joins the first (this ramus is present in a high percentage of cases) is recognized as a nerve through which sympathetic fibers arising in the second and lower thoracic sympathetic trunk ganglions enter the upper extremity. The ramus arising from the third thoracic nerve and joining the second, described in the present paper, occurs somewhat less frequently than the one arising from the second thoracic nerve and joining the first. It also includes a relatively high percentage of sympathetic fibers, many of which undoubtedly continue upward in the latter ramus and enter the ramus of the first thoracic nerve which joins the brachial plexus. A pathway is thus provided through which sympathetic fibers which leave the sympathetic trunk through the gray communicating ramus of the third thoracic nerve may enter the upper extremity without traversing gray communicating rami which join the first thoracic or cervical nerves. In order to interrupt this pathway by cervicothoracic sympathectomy it would be necessary to extend the operation downward to include extirpation of the third thoracic sympathetic trunk ganglion.

In view of the anatomic relations of the cervicothoracic and low middle cervical sympathetic ganglions, cervicothoracic sympathetic ganglionectomy does not necessarily involve extirpation of the low middle cervical ganglion. In certain cases, as observed in the present investigation, the communicating rāmus of the eighth cervical nerve is connected with both the cervicothoracic and the low middle cervical ganglion. In some of these cases, this communicating ramus included some myelinated components which probably were preganglionic fibers which emerged from the spinal cord via the eighth cervical nerve. The continuity of the part of this ramus which joins the low middle cervical ganglion is not necessarily interrupted by extirpation of the cervicothoracic ganglion. In case it should be interrupted, any preganglionic fibers present might regenerate into the low middle cervical ganglion. Although the communicating ramus of the eighth cervical nerve probably conveys preganglionic fibers only in a low percentage of cases, it may in certain cases play a role in the sympathetic innervation of the upper extremity.

In view of all the anatomic data available, complete sympathetic denervation of the upper extremity by sympathetic ganglionectomy requires extirpation of the cervicothoracic and lower sympathetic trunk ganglions, including the second and third thoracic, in a relatively high percentage of cases. In certain cases, i. e., those in which the communicating ramus of the eighth cervical nerve includes preganglionic fibers, it may be necessary also to remove the low middle cervical ganglion.

WASH BASIN CONTAMINATION IN OPERATING ROOMS

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This bacteriologic investigation of contamination was occasioned by a recent change of solutions in the wash basins in the operating rooms of the New Haven Hospital. The weak bacteriostatic solution of iodine used previously was changed to sterile water in quantities of 1,000 cc. in each large shallow basin placed behind an operator, in which the operator washes off his gloves during the operative procedure. This change was made in the hope that discontinuance of the use of the iodine solution would decrease the dermatitis prevailing among the operating staff.

In a few cases a disinfectant, zephiran,[1] was put in the basins in a concentration of 1 : 5,000 in sterile water. This was done only when contamination of the basins during the operative procedure was most likely.

TECHNIC

The technic employed throughout these investigations was as follows: At the close of the operation 1 cc. of fluid was removed with a sterile pipet from either one or both wash basins. A pour plate was made with 10 cc. of melted beef infusion agar mixed with the 1 cc. portion of the fluid. In the instances in which zephiran was used this procedure gave a concentration of zephiran in the medium of 1 : 50,000.

Each culture was incubated at 37 C. for forty-eight hours, and then the colony counts were made and recorded. The following items were also noted: the name of the patient, the operator, the type of operation, the period over which the basins were exposed, whether the wound was considered contaminated and drained and, finally, whether any acute or gross infection was present one week after operation.

The cases hereinafter reported were selected at random so that examples of the main types of surgical procedure might be included. A large majority of the cases were selected because of the probability

1. Zephiran is alkyldimethylbenzylammonium chloride. It is a cationic detergent having about the same consistency and physical properties as liquid soap, which is an anionic detergent.

that the fluid in the wash basins would become contaminated but only when such contamination would be important with respect to wound healing. For this reason all cases in which an abscess was drained and all cases in which rectal conditions were dealt with were eliminated. However, no results were rejected after a case was once selected.

CONTROL EXPERIMENTS

Control cultures to demonstrate the bacteriostatic action of zephiran were made by injecting single loopfuls of a beef broth culture of Staphylococcus aureus or Streptococcus viridans into tubes of melted agar. A series of tubes was used which contained dilutions of zephiran ranging from 1 : 10,000 to 1 : 100,000, as well as control tubes without

TABLE 1.—*Bacteriologic Results of Control Cultures Made to Demonstrate the Bacteriostatic Action of Zephiran*

Dilution of Zephiran Used	Organisms	
	Staphylococcus Aureus	Streptococcus Viridans
1:10,000	0	0
1:20,000	0	0
1:30,000	0	0
1:40,000	0	0
1:50,000	0	0
1:60,000	0	0
1:70,000	0	0
1:80,000	Grade 1	0
1:90,000	Grade 1	Grade 1
1:100,000	Grade 1	Grade 1
Control tubes without zephiran	..	Grade 4

any zephiran. Growth in the control plates was measured from grade 1 (having less than five colonies per plate) to grade 4 (having innumerable colonies).

RESULTS

(1) Cases in which cultures were made 22
(2) Basins from which 1 cc. samples were cultured 39
(3) Cases in which viable bacteria were obtained from at least one basin .. 13
(56 per cent of all cases; 76 per cent of cases in which zephiran was not used)
(4) Basins containing viable bacteria ..... 19 (49 per cent)

(5) Cases in which zephiran was used in basins ..... 5 (23 per cent)
(6) Cases in which basins with zephiran yielded viable bacteria 0

(7) Cases in which wound was considered contaminated and drained ..... 10 (45 per cent)
(8) Basins used in cases in which drainage was done ..... 18 (46 per cent)
(9) Drainage cases in which basins contained viable bacteria .. 5 (50 per cent)
(10) Drainage cases in which zephiran was used in basins ..... 3 (30 per cent)

(11) Cases in which drainage was not done ..... 12 (55 per cent)

(12) Basins used in cases in which drainage was not done..... 21 (54 per cent)
(13) Nondrainage cases in which basins contained viable bacteria ..... 8 (36 per cent)
(14) Nondrainage cases in which zephiran was used in basins.. 2 (17 per cent)

(15) Longest period of exposure after which basin remained sterile without use of zephiran.....3½ hours

(16) Controls 22
Percentage of stock cultures sterilized by zephiran in 1: 50,000 solution 100
Lowest dilution of zephiran in which bacteria grew..... 1: 80,000

(17) Quantitative estimate of contamination:
Cases in which viable bacteria were obtained from basins.. 13 (49 per cent)
Cases in which colony count exceeded 5 per cubic centimeter ..... 9 (41 per cent)
Cases in which colony count exceeded 10 per cubic centimeter ..... 4 (18 per cent)
Cases in which colony count exceeded 40 per cubic centimeter ..... 2 (9 per cent)

(18) Predominating types of bacteria found in basins.....
.....Bacillus coli, Staphylococcus aureus, Bacillus proteus

(19) Selected cases in which there was an acute wound infection or a breakdown of a drained wound..... 0

COMMENT

The discrepancy in several instances between the heavy infection of basins in some cases and the complete sterility in other apparently similar cases (zephiran being absent in both) may be accounted for by the fact that members of the senior surgical staff ordinarily rinse their hands in the basins a great many more times during an operation than members of the junior staff. A few of the basins, judging from the clean appearance of the water at the end of the operation and the sterility of the water, had not been used much, if at all, during the operative procedures. The same explanation applies to the fact that one basin in certain operations would be heavily contaminated and the other remain sterile. In these cases the operator usually remained on one side of the table, and the assistants did not use the other basin. This irregularity in the contamination of the two basins used in a single operation is the reason why the results are reported according to the number of cases rather than according to the number of contaminated basins.

The fact that some of the basins without zephiran remained sterile when exposed to the room air for as long as three and a half hours, apparently not used, serves to act as a control on the origin of the contamination. This is interpreted as evidence that the contamination

came primarily from the operator's hands and instruments rinsed in the basins and not from the air.

The fact is significant that 56 per cent of the total number of cases studied, or 76 per cent of the cases without antiseptic solution in the basins, showed sufficient numbers of viable bacteria, ranging from 1 to

TABLE 2.—*Data on Twenty-Two Cases in Which Cultures Were Made with Samples from the Fluid in the Wash Basins Used at Operation*

Case	Surgical Staff of Which Operator was Member	Operation	Time of Operation, Hr.	Colony Count	Dirty Fluid in Basin	Zephiran 1:50,000, Used	Postoperative Infection
1	Senior	Exploratory laparotomy	1	6	0	0	0
2	Senior	Resection of the colon	1½	0	0	+	0
3	Senior	Exploratory thoracotomy	1½	3	+	0	0*
4	Senior	Cholecystectomy	1½	6	+	0	0*
				18	+	0	
5	Junior	Excision of the submaxillary gland	1½	0	0	0	0
6	Junior	Leg amputation (guillotine)	1	0			Wound left open
				20	+	0	
7	Senior	Spinal fusion	2½	8	0	0	0
				4		0	
8	Senior	Trephining	2	1	..	0	
				2	0	0	0
9	Junior	Cholecystotomy	1¾	0	+	+	0*
10	Senior	Craniotomy	3	0	0	0	0
			6	5		0	
				3		0	
11	Senior	Colectomy	4	0	+	+	0
12	Senior	Spinal fusion	3	0	0	+	0
				0		+	
13	Senior	Exploratory operation on the kidney	2	0	+	0	0
				0		0	
14	Junior	Colectomy	3½	0	+	0	0*
15	Senior	Lumbar sympathectomy	3	50	0	0	0
				0		0	
16	Junior	Cholecystectomy	1½	1	+	0	0*
				6		0	
17	Junior	Hernia	1½	0	0	0	0
				0		0	
18	Junior	Thyroidectomy	3½	6	0	0	
					0	0	0
19	Senior	Exploratory operation on the common duct	2½	0	..	+	
				0	+	+	0
20	Junior	Hysterectomy	2	0	0	0	0
				2		0	
21	Senior	Exploratory laparotomy	2	1	0	0	0
				0		0	
22	Senior	Colectomy	4	40	..	0	
				13	+	0	0*

* Drainage was done.

50 organisms per cubic centimeter of fluid withdrawn from the wash basins, to be a definite hazard to aseptic technic and wound healing.

The complete absence of viable bacteria in all the cultured samples from the basins containing zephiran is in marked contrast to the contamination of 76 per cent of the basins without zephiran.

The absence of any badly infected wounds in the series is somewhat surprising in view of the high bacterial counts for some of the basins.

The fact that in 46 per cent of the cases the wound was drained probably eliminated some of the potential infections from contaminated basins. The basins in 36 per cent of the cases in which the wound was not drained were contaminated.

The cost (estimated at about $10 a day) of supplying 400 cc. of the 1:1,000 stock solution of zephiran for each operation in a busy operating room is probably prohibitive. Some less expensive antiseptic which would be bactericidal in a dilution weak enough to eliminate dermatitis is almost essential to maintain a suitable aseptic technic.

Admittedly, the series of 22 cases studied is too small to permit any final conclusions as to the relation of contamination of the wash basins to the incidence of wound infection.

CONCLUSIONS

The wash basins in which the operators cleanse their hands in the operating room are frequently the most contaminated spots in the whole sterile setup.

The contaminated wash basins, used throughout the operation, act as a potential source of infection of the wound edges when these are closed and may account for the breakdown of a certain number of incisions.

An antiseptic solution should be placed in the wash basins in at least all cases in which a major operation is to be performed on the abdomen. The hands during intestinal manipulations in most of these cases become potential sources of infection but should be sterile while the abdominal wall is being closed. The antiseptic solution should be nonirritating to the operator's hands. It should be inexpensive, so that it can be used freely and so that the basins can be changed several times during a long operation. It should be used in sufficient concentration to be bactericidal in a few minutes in order to combat the moderate amount of contamination which is ordinarily introduced into the basins. Mere bacteriostatic action of an antiseptic in the basins is insufficient if the organism remains viable when cultured in vivo.

The average incision is apparently able to combat successfully a large amount of contamination without becoming infected. This is shown by the primary closure of all operative wounds except the drainage sites in all the cases reported (except a case in which the guillotine amputation was performed) despite relatively heavy contamination of the basins.

THE TWO STAGES OF BOWEL DISTENTION

A STUDY OF BOWEL INJURY BY DISTENTION AND ITS EFFECT ON THE VOLUME AND CONCENTRATION OF THE BLOOD

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AND
J. S. BATTERSBY, M.D.
INDIANAPOLIS

What distending pressure will injure the bowel? All writers agree that injury done to the bowel by distention affects chiefly its circulation. The answer to this question should therefore be indicated by the fundamental relation between the volume of blood flowing through the wall of the bowel and the pressure within its lumen. This relation is that the volume of blood flowing through the wall of the bowel decreases as the intraintestinal pressure increases, until it becomes nothing when the intraintestinal pressure is equal to the systolic blood pressure.[1] A corollary to this is the fact that a continuous flow of blood ceases when the intraintestinal pressure exceeds the diastolic blood pressure. Then a flow through the blood capillaries occurs only during ventricular systole. Proof of the critical importance of the relation between the intraintestinal pressure and the diastolic blood pressure is that intes-

1. (*a*) Gatch, W. D.; Trusler, H. M., and Ayers, K. D.: Effects of Gaseous Distention on Obstructed Bowel, Arch. Surg. **14**:1215-1221 (June) 1927. (*b*) Dragstedt, C. A.; Lang, V. F., and Millet, R. F.: The Relative Effects of Distention on Different Portions of the Intestine, ibid. **18**:2257-2263 (June) 1929. (*c*) Dragstedt showed that the decrease in blood flow, which he recorded in percentages of the normal flow, is most marked in the duodenum and least marked in the colon. He gave an anatomic explanation for this based on the demonstration by Eisberg that from the duodenum to the colon the points at which the vasa recta pierce the muscularis of the bowel are situated farther and farther from the mesenteric border of the bowel. They are near the mesenteric border of the duodenum and in the amesenteric quadrants of the colon.

We doubt the validity of this explanation, because the impairment of the circulation is evidently due to compression of the bowel capillaries, and we cannot see how the points at which the vasa recta pierce the muscularis of the bowel can have any effect on this. The anatomic explanation we favor is that there is a gradual decrease in the thickness of the mucosa from the duodenum to the colon. The submucous coat of the bowel offers most of the resistance to distention, and the mucosa surrounded by it is compressed more by distention than is the muscularis. Therefore, the effect of distention will be most marked where the mucosa is thickest (i. e., in the duodenum) and least marked where the mucosa is thinnest (i. e., in the colon).

tinal function, as shown by the power of absorption, ceases when the intraintestinal pressure equals or exceeds the diastolic blood pressure.[2]

The blood flow through the intestinal wall depends not only on the intraintestinal pressure but also on the diastolic blood pressure. For example, when the diastolic blood pressure is 80 and the intraintestinal pressure 60 mm. of mercury, there will be a fairly large flow of blood. However, this flow will not be continuous if the diastolic blood pressure sinks to 60, as the pressure often does in patients with advanced obstruction. Then the pulse pressure also may be low, and the flow of blood will almost cease.

Few direct measurements of intraintestinal pressures have been made. Those recorded vary from 13 to 111 mm. of mercury.[3] The facts are: (1) that except for extremely high pressures the intraintestinal pressure alone is no measure of the impairment of circulation; (2) that a pressure high enough to put the wall of the bowel under tension will decrease in the course of a few hours because of dilation of the bowel; (3) that the color of the wall of the bowel and its degree of tensity clearly show whether the pressure is injuring it.

Experiments show that a pressure great enough to cause tenseness of the wall of the bowel will slowly decrease as the bowel dilates and becomes flaccid; that a tense bowel has a greatly diminished blood flow; that a flaccid bowel has enough blood flow to keep it alive, though it suffers from congestion of blood in its capillaries. Thus dilation protects the bowel against high intraluminal pressure, provided the pressure does not increase step by step with the dilation.

These observations on the experimental animal are similar to those made at operation for obstruction of the bowel in man. We find clinically that the bowel for a variable distance proximal to an obstruction is always dilated. In some cases it is tense, dry and pale; in other cases it is flaccid, edematous and blue. Here also, the tense pale bowel is being injured, and the flaccid blue bowel is convalescing from injury. The significant pressure, that is, the pressure which damages the bowel, is the pressure within the tense pale bowel. We know by deduction and experiment that this must be near the diastolic blood

2. Gatch, W. D.; Owen, J. E., and Trusler, H. M.: The Effect of Distention of the Bowel upon Its Circulation and upon Absorption from Its Lumen, West. J. Surg. **40**:161-170, 1932.

3. Stone, H. B., and Firor, W. M.: Absorption in Intestinal Obstruction: Intra-Intestine Pressure as a Factor, Tr. South. S. A. **37**:173-184, 1924. Sperling, L.; Paine, J. R., and Wangensteen, O. H.: Pressure in Experimental and Clinical Intestinal Obstruction, Proc. Soc. Exper. Biol. & Med. **32**:1504-1506, 1935. We once observed rupture of a distended loop of bowel on its escape from the abdomen. We found by experiment that a piece of fresh human ileum ruptured at a pressure of 210 mm. of mercury.

pressure. Flaccidity and blueness of a distended bowel show that at one time there was a high pressure within it.

We do not deny that the bowel is somewhat injured by a prolonged pressure as low as 22 mm. of mercury or that prolonged inflation of long stretches of the small bowel at this level of pressure will cause death, but we do deny that this pressure acting continuously for twelve hours or more will cause any significant change in the vitality or the structure of the bowel. Analysis of Sperling's experiments supports this conclusion. We have demonstrated this by a number of experiments. The clinical and the experimental evidence both support the conclusion that acute and serious injury to the bowel by intraintestinal pressure occurs only when this pressure is near the diastolic blood pressure and persists for several hours.

The foregoing considerations guided us in planning our experiments.

PROTOCOLS OF EXPERIMENTS

SERIES 1 (8 dogs).—*Experiments Designed to Show the General Effects of Distention on the Bowel.*—Sodium amytal was given intravenously to induce anesthesia. A piece of the small intestine was delivered through a short incision, gently stretched and divided into three segments of equal length (20 cm. each), careful allowance being made for the small lengths of bowel necessary for ligation. One segment was excised and weighed. The remaining segments were inflated with pressures ranging from 22 to 74 mm. of mercury in different experiments. Pressure was maintained for four hours, then released in one segment but maintained in the other for thirty minutes more. Then both segments were excised and weighed.

Results.—Segments in which pressure was maintained throughout the experiment decreased on the average about 2 Gm. in weight. Segments in which the pressure was released during the final thirty minutes of the experiment showed an increase of approximately 20 per cent of their original weight. Segments in which the pressure was maintained throughout the experiment remained dry and pale; segments in which pressure was released thirty minutes before the close of the experiment became dusky and edematous.

Practically no fluid was found in the lumens of any of the loops. Drops of fluid were seen over the surfaces of all distended loops. Analysis of this fluid showed that it contained: total protein, 3.7 per cent; albumin, 3.2 per cent; globulin, 0.5 per cent.

Sections for microscopic study of the segments kept inflated throughout the experiments showed compression of the tissues, especially of the mucosa, and absence of blood in the capillaries and the veins. Sections of segments deflated thirty minutes before the close of the experiments showed edema of the mucosa, slight loss of epithelium or no loss at all, slight extravasation of blood, considerable accumulation of blood in the capillaries and veins and great edema of the fat at the mesenteric border of the bowel.

Conclusions.—Our conclusions from this series of experiments are: (1) that an intraintestinal pressure of 22 mm. of mercury or more maintained for several hours decreases the quantity of fluid in the

wall of the bowel and that, up to a certain limit, the greater the pressure, the greater the decrease of fluid; (2) that part of this loss of fluid is due to a sweating of albuminous fluid from the peritoneal surface of the bowel, and (3) that a piece of bowel which has been kept distended for several hours increases in weight and becomes markedly edematous and cyanotic after the distention is released.

SERIES 2 (4 dogs).—*Experiments to Determine the Cause of the Increase in Weight of the Bowel Following the Release of Pressure.*—In this series we repeated the experiments just described except that we injected 20 cc. of a 1 per cent solution of trypan blue into the femoral vein thirty minutes before the close of the experiments, at the time the pressure was released from one of the segments.

Results.—Within two or three minutes after the injection of the dye, the deflated segments of the bowel started to turn blue, and this color darkened progressively until the end of the experiment. Segments which were kept inflated and the untreated intestines showed no change in color.

We had to consider that the trypan blue in the damaged bowel might be entirely in the capillaries and not in the tissue spaces. It is impossible to demonstrate microscopically the extravasation of trypan blue into the tissue, for during the process of fixation the dye diffuses out. We obtained conclusive proof of abnormal capillary permeability by observing a blue stain on blotting paper held against the bowel.

In some experiments a suspension of india ink was used instead of trypan blue. Microscopic study of the bowel in the experiments in which the india ink was used revealed the presence of edema in all coats of the bowel and in the mesenteric fat. The epithelium of the mucosa showed little or no change from normal. There were small hemorrhages in the submucous coat. The blood vessels were dilated and in some instances outlined by india ink adherent to their walls. In other areas the blood vessels contained clumps of india ink. In all parts of the sections studied particles of india ink could be identified in the tissues, especially in the mesenteric fat, and in the submucous and muscular coats of the bowel.

Conclusions.—Distention of the bowel by pressures which impede the circulation in the wall to a considerable degree for several hours damages the capillaries so that they become permeable to the blood proteins. This leads to an escape of blood proteins into the tissues of the bowel after the release of pressure. Therefore a part of the increase in weight of the bowel after the release of distention is due to edema caused by the escape of plasma from capillaries. The other part must be due to the excessive quantity of blood in the capillaries.[4]

Why does blood accumulate in the capillaries of a bowel in the second stage of distention? We once held the common opinion that distention of the bowel causes obstruction to the venous outflow of the bowel. We suggested that the accumulation of blood might be due to

4. Sperling, L.: Mechanics of Simple Intestinal Obstruction: An Experimental Study, Arch. Surg. **36**:778-815 (May) 1938.

torsion of the mesenteric veins and to pressure on them by distended loops of the bowel.[5] Direct observation of the effects of distention of the bowel on the mesentery convinced us that this explanation is not true. We therefore looked for another.

It occurred to us that the cause of the congestion observed in the second stage of distention of the bowel might be vasomotor paralysis of the arterioles in the wall of the bowel. We have been unable to find any report on this effect of distention. We made the following observations a number of times in the course of experiments for other purposes: (1) When a segment of the bowel is kept tense for several minutes by inflation and then suddenly deflated, it suddenly assumes a bright red color which contrasts sharply with the paler hue of the bowel on each side of it. The bright color fades in a few minutes. This effect is the same as that observed on the skin of the forearm after the release of a tourniquet placed around the arm. (2) When the bowel is kept tense for several hours and then deflated, it becomes and remains cyanotic. The first effect is due to a temporary vasomotor paralysis; the second, to a more lasting one.

SERIES 3 (10 dogs).—*Experiments to Determine the Quantity and the Composition of the Fluid Found in the Peritoneal Cavity as a Result of Distention of the Bowel.*—Control Experiment: Sodium amytal was given intravenously to a dog to induce anesthesia. Laparotomy was then performed. The pylorus was ligated. The terminal part of the ileum was divided and a tube inserted into the proximal end. The tube was brought out through the abdominal incision which was then closed. The experiment occupied four hours. No fluid could be collected from the peritoneal cavity.

Experiments: Various experiments were performed in which the procedures outlined for the control experiment were carried out and in which in addition the bowel was inflated with pressures ranging in different experiments from 22 to 100 mm. of mercury. In each experiment only one pressure was used, and this was maintained constantly for six hours.

Results.—The results of these experiments are shown in detail in table 1.

Conclusions.—The quantity of fluid in the peritoneal cavity as a result of distention of the bowel tends to increase as the pressure in the bowel increases. It also tends to increase with the duration of the distention (see data on dogs 2 and 10 in table 1). Analysis shows that this fluid contains approximately half as much protein as the blood plasma and relatively more than half as much albumin. In protein content the fluid is equal to about half its volume of plasma. Dog 8, for example, lost about one fifth of its total quantity of blood protein in the peritoneal fluid.

5. Gatch, W. D., and Culbertson, C. G.: Circulatory Disturbances Caused by Intestinal Obstruction, Ann. Surg. **102**:619-635, 1935.

A considerable quantity of intraperitoneal fluid is always found in human patients with obstruction of the bowel. Recently, in a patient with obstruction due to a gallstone impacted in the lower part of the ileum, we found a large quantity of this fluid; analysis showed the following composition: total protein, 4.2 per cent; albumin, 3.4 per cent; globulin, 0.8 per cent. These percentages are a little higher than those for the fluid obtained from experimental animals.

TABLE 1.—*Data on Experiments to Determine the Quantity and the Composition of the Fluid Found in the Peritoneal Cavity as a Result of Bowel Distention*

Dog	Weight of Dog, Kg.	Intra-intestinal Pressure, Mm. of Mercury	Duration of Experiment, Hr.	Amount of Fluid Collected, Cc.	Analysis of Fluid		
					Total Protein, per Cent	Albumin, per Cent	Globulin, per Cent
1	12.9	22.0	6	50			
2	12.1	29.0	6	100			
3	10.0	29.6	6	125	4.5	2.9	1.6
4	14.0	33.0	6	85			
5	13.0	44.0	6	150	3.0	2.3	0.7*
6	13.0	59.0	6	150	2.8	2.2	0.6
7	12.5	62.0	6	155	3.6	2.7	0.9
8	13.0	74.0	6	200			
9	10.0	100.0	6	250			
10	15.0	29.0	16	195			

* Analysis of the blood plasma of this dog showed: total protein 7.1 per cent; albumin, 4.2 per cent; globulin, 2.9 per cent.

TABLE 2.—*Data on Experiments to Determine the Origin of the Fluid Found in the Peritoneal Cavity in the Presence of Distention of the Bowel*

Dog	Experiment	Weight of Dog, Kg.	Length of Bowel Segments, Gm.	Weight of Segment *A*, Gm.	Weight of Segment *B* at the Close of the Experiment, Gm.	Increase in the Weight of the Gauze, Gm.	Pressure, Mm. of Mercury	Hematocrit Determinations, per Cent		Time, Hr.
								Initial	Final	
1	1	13.8	30.0	22.0	21.9	5.0	50	48	54	3
2	2	5.7	16.5	20.5	20.5	4.0	22	..	..	3
2	3	...	16.5	20.5	17.1	6.1	44	..	..	3
2	4	...	16.5	20.5	19.0	10.0	74	..	..	3

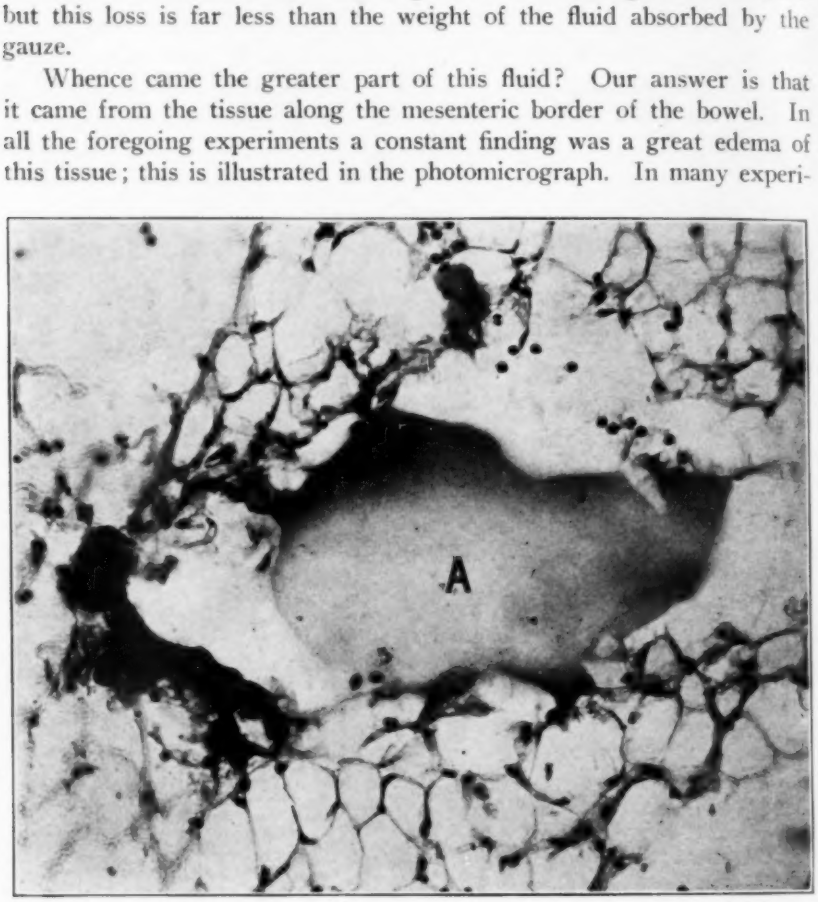
SERIES 4 (2 dogs).—*Experiments to Determine the Origin of the Fluid Found in the Peritoneal Cavity in the Presence of Distention of the Bowel.*—Anesthesia was induced with sodium amytal and laparotomy performed. Two contiguous segments of bowel of equal length were used for each experiment. One segment (*A*) was excised and weighed; the other (*B*) was kept inflated to a constant level of pressure, having first been wrapped in dry weighed gauze. At the end of the experiment the gauze and segment *B* were each weighed.

Results.—The results of these experiments are given in table 2. Analysis of the fluid wrung from the gauze used in experiments 2 and 3 showed: total protein, 3.7 per cent; albumin, 3.2 per cent; globulin, 0.5 per cent.

Conclusions.—Our conclusions from this series of experiments are: (1) that the peritoneal fluid comes in part from the distended bowel;

(2) that the quantity of the fluid increases as the intraintestinal pressure increases (experiments 2, 3 and 4 were all done on the same dog); (3) that constant distention causes a slight loss in the weight of the bowel but this loss is far less than the weight of the fluid absorbed by the gauze.

Whence came the greater part of this fluid? Our answer is that it came from the tissue along the mesenteric border of the bowel. In all the foregoing experiments a constant finding was a great edema of this tissue; this is illustrated in the photomicrograph. In many experi-



Photomicrograph of the fat at the mesenteric border of a bowel which had been kept tightly distended for some time. *A*, edematous fluid.

ments the mesenteric border of the bowel was ½ inch (1.2 cm.) thick, and fluid dripped from it when it was cut. In experiment 2 of series 4 the pressure used was 77 mm. of mercury. The weight of the gauze increased 10 Gm., and that of the bowel decreased 1.5 Gm. Therefore, 8.5 Gm. of the fluid absorbed by the gauze must have come from the mesenteric fat, since there was no other source for it. With a lower intraintestinal pressure it is probable that the part of the fluid derived from the bowel would be relatively greater.

There is, we believe, a complete and satisfactory explanation for the edema of the fat at the mesenteric border of the bowel.

Gatch, Trusler and Ayers [1a] observed that there is always some flow of blood, which no degree of intraintestinal pressure will stop, from the vein which drains a distended loop of bowel. They attributed this to small anastomotic arteries at the mesenteric border. Dragstedt [1b] concurred in this explanation and recorded the observation that with maintenance of distention the flow in question gradually increases until it equals the flow through the unobstructed bowel. This explains the maintenance of the flow of blood through the mesentery when circulation through the intestine is arrested by distention. It accounts also for the exudation of fluid from the capillaries at the mesenteric border in the presence of bowel distention, because then these capillaries must dilate to make room for a much greater volume of blood than that to which they are accustomed.

SERIES 5.—*Experiments to Determine Whether After the Release of Prolonged Distention There Is a Loss of Blood Proteins into the Tissues and Mesentery of the Bowel and into the Peritoneal Cavity Sudden Enough and Great Enough to Cause Concentration of the Blood.*[6]—Experiment 1: The entire small intestine of a dog was kept inflated with a pressure of 44 mm. of mercury for four and a half hours.

The hematocrit reading at the start of the experiment was 49 per cent; after four and a half hours of inflation it was 55 per cent; fifteen minutes after deflation it was 57 per cent; thirty minutes after deflation it was 59 per cent.

Experiment 2: The entire small intestine of a dog was kept inflated with a pressure of 71 mm. of mercury for four hours. The hematocrit reading at the start of the experiment was 41 per cent; after four hours of inflation it was 60 per cent; thirty minutes after deflation it was 63 per cent.

Experiment 3: The entire small intestine of a dog was kept inflated with a pressure of 61 mm. of mercury for six hours. The hematocrit reading at the start of the experiment was 42 per cent; after six hours of inflation it was 66 per cent; fifteen minutes after deflation it was 68 per cent.

Experiment 4: The entire small intestine of a dog was kept inflated with a pressure of 71 mm. of mercury for four hours. The hematocrit reading at the start of the experiment was 41 per cent; after four hours of inflation it was 60 per cent; thirty minutes after deflation it was 63 per cent; at intervals of thirty minutes for a period of two hours it remained 59 per cent.

Experiment 5: The entire small intestine of a dog was kept inflated with a pressure of 50 mm. of mercury for four hours. The hematocrit reading at the start of the experiment was 45 per cent; after four hours of inflation it was 61 per cent; then for five determinations made at intervals of thirty minutes it remained 63 per cent.

Conclusions.—The results indicate that after deflation of a small bowel which has been tightly distended for four hours there is a slight

6. Elman, R.: The Danger of Sudden Deflation of Acute Distended Bowel in Late Low Intestinal Obstruction, Am. J. Surg. **26**:438-446, 1934. Ochsner, A., and Storck, A. H.: Mechanical Decompression of the Small Intestine in Ileus, J. A. M. A. **108**:260-266 (Jan. 23) 1937. Fine, J.; Fuchs, F., and Gendel, S.: Changes in Plasma Volume Due to Decompression of the Distended Bowel, Arch. Surg. **40**:710-716 (April) 1940.

increase in the concentration of the blood. It seems certain that this concentration is due to the escape of blood plasma into the tissue spaces of the deflated bowel. We had the idea that this concentration might be great enough and sudden enough to explain death which sometimes follows shortly after deflation of a distended bowel in man, but the increases in the blood concentration which we observed in these experiments were too small to lend much support to this hypothesis. It next occurred to us that in addition to this loss of plasma the circulation would lose a considerable quantity of whole blood pooled in the capillaries of the deflated bowel. With this thought in mind we repeated the foregoing experiments on 2 dogs and measured the blood volume before and after deflation. The loss in blood volume was so small that it came within the experimental error of the method. It is well known, however, that the determination of the blood volume in the presence of hemoconcentration or of an impairment of circulation due to other causes is inaccurate. Simple inspection shows that the deflated bowel contains an abnormal amount of poorly oxygenated blood. The experiments in series 1 showed that the bowel on deflation after four to six hours of tight inflation increases in weight by about 20 per cent. The small intestine of a dog is about 320 cm. in length. We determined by many estimations that its weight on the average is about 1 Gm. per centimeter. An increase of one fifth of this weight would require 75 to 100 cc. of blood and plasma. We believe that this is an accurate estimate of the loss of blood and plasma from the circulation following deflation. When the circulation of an animal is in a precarious condition owing to hemorrhage or hemoconcentration, it is well known that a comparatively small loss of blood is fatal. Therefore, we think it reasonable to believe that death following shortly after the sudden deflation of long pieces of a distended bowel may in some cases be explained by the pooling of blood in the deflated bowel.

The foregoing remarks apply to the effects of deflating a bowel in the first stage of distention. The deflation of a bowel in the second stage of distention by the operation of stripping might be fatal by reason of hemorrage into the wall of the lumen of the bowel. The tissues of a bowel in the second stage of distention are extremely weak and bleed freely.

SUMMARY AND CONCLUSIONS

Injury to the bowel by distention depends not only on the distending pressure but also on the diastolic blood pressure. Pressures less than half the diastolic blood pressure do but little injury to the bowel unless they act continuously for a long time.

Distention great enough to injure the bowel tends to pass through two stages which are clearly defined in both human beings and experimental animals. The bowel is tense and anemic in the first stage and

flaccid and congested in the second. It passes from the first to the second stage when its wall stretches enough to permit resumption of flow of the blood in fair volume through its capillaries. It is being injured in the first stage; it is recovering from this injury in the second. Failure to recognize the occurrence of these two stages has led to much error in the interpretation of results of experiments on distention.

Most of the albuminous fluid found in the peritoneal cavity in the presence of bowel obstruction accumulates there in the first stage of distention. Some of it is squeezed out of the bowel wall, but the greater part escapes from the fat along the mesenteric border of the bowel.

The quantity of this fluid varies with the duration of the first stage of distention and with the degree of obstruction to the flow of blood in the wall of the bowel attendant on distention.

The protein content of the peritoneal fluid is about half that of plasma and consists chiefly of albumin. Damage to the capillaries by distention is evidently not so serious as that due to burns or inflammation which makes the capillary endothelium incapable of holding back the large globulin molecules.

No fluid accumulates in the lumen of the bowel in the first stage of distention; our experiments do not show whether it accumulates in the second stage.

The cyanosis of the bowel in the second stage of distention is due to vasomotor paralysis and to the relaxation of the tissues which support the capillaries. It is not due to venous obstruction.

CLINICAL APPLICATIONS

The quantity of albuminous fluid lost to the circulation because of the effects of distention on the bowel is probably of no great importance except in cases of rapidly developing and great distention. When the distention develops slowly, the body can probably produce blood protein as rapidly as it is lost. Our clinical observation supports this idea.

In cases of intestinal obstruction in man both stages of distention may be present. The part of the bowel immediately above an obstruction which has been present for some time may be in the second stage of distention; the part of the bowel above this may be in the first stage. At a still higher level the bowel may be found dilated, although it may not be dilated enough to prevent it from contracting. Pressure is not the same in all parts of the intestine.

Death occurring shortly after the rapid deflation of a distended bowel may be due in some cases to a sudden loss of blood and plasma from the circulation.

Our observations seem to indicate that the best treatment of intestinal obstruction is intestinal intubation, followed by enterostomy if at operation the bowel is found in a badly damaged condition. A bowel

in the second stage of distention cannot contract or perform any of its functions in a normal way. Therefore, actual removal of the cause of obstruction may not relieve the obstruction until a long time afterward.

Our experiments were confined to the effects of distention on the small bowel, but we believe that with certain reservations the conclusions apply to the large bowel as well. In man the large bowel can be tremendously dilated without much interference with its circulation, but once the pressure within it approaches the diastolic blood pressure, the large bowel will, there is every reason to believe, suffer the same damage as the small bowel. Surgeons do not often observe this damage to the large bowel because of the latter's distensibility and because as a rule distention increases slowly and is relieved by colostomy before it does serious harm. However, most surgeons have observed at operation or autopsy rupture of the large bowel caused by distention.

RIB RESECTION IN THE TREATMENT OF SCOLIOSIS

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Although there have been some satisfactory results obtained by the use of the more recently developed method of treatment for scoliosis (particularly by the turnbuckle jacket with eventual fusion of the primary curve), these procedures still leave much to be desired. Because of the small percentage of really good results, the prolonged period of hospitalization and the consequent high cost of the treatment, a more satisfactory method would indeed be welcome.

The treatment of scoliosis by rib resection was originally suggested to Hoffa [1] by Volkmann [2] in 1889. In this country in 1902, Hoke [3] performed rib resection on a 16 year old girl with a high right dorsal curve (the apex was at the level of the eighth thoracic vertebra). He had tried postural treatment and braces unsuccessfully before operating. The prominence of the ribs extended from the fourth rib down on the right side. After trying rib resection on a cadaver, he operated on the patient. This was done in three stages.

The first stage consisted of resection of the fifth to the eighth ribs inclusive, on the left side. Hoke justified his procedure by saying that:

> . . . as long as that area was sunken in, the plane of the chest wall would be such that the left shoulder must glide backwards towards the spine; and because the position of these ribs and their attachment to the spine opposed structurally the counter-rotation efforts.

Six weeks later he performed osteotomy of the ribs on the right side and resected five ribs. Four months later the third operation was done.

No roentgenograms were made at that time, but the published photographs look good.

The procedure was certainly considered radical and was likely associated with a great deal of shock to the patient. The first stage took three and a half hours to perform.

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1. Hoffa, A.: Operative Behandlung einer schweren Skoliose (Resection des Rippenbuckels), Ztschr. f. orthop. Chir. **4**:402-408, 1895-1896.

2. Volkmann, R.: Rippenresection bei der Skoliose, Berl. klin. Wchnschr. **26**:1097, 1889.

3. Hoke, M.: A Study of a Case of Lateral Curvature of the Spine: A Report on an Operation for the Deformity, Am. J. Orthop. Surg. **1**:168-208, 1903-1904.

In more recent years, when rib resection had become a common procedure in the treatment of tuberculosis, it was immediately noted that in many of the patients some curvature of the spine developed as a result of thoracoplasty.

In 1934, Bisgard,[4] working in the field of thoracic surgery, reported a series of cases and pointed out some important facts. He was chiefly concerned with preventing scoliosis after rib resection, and he stated

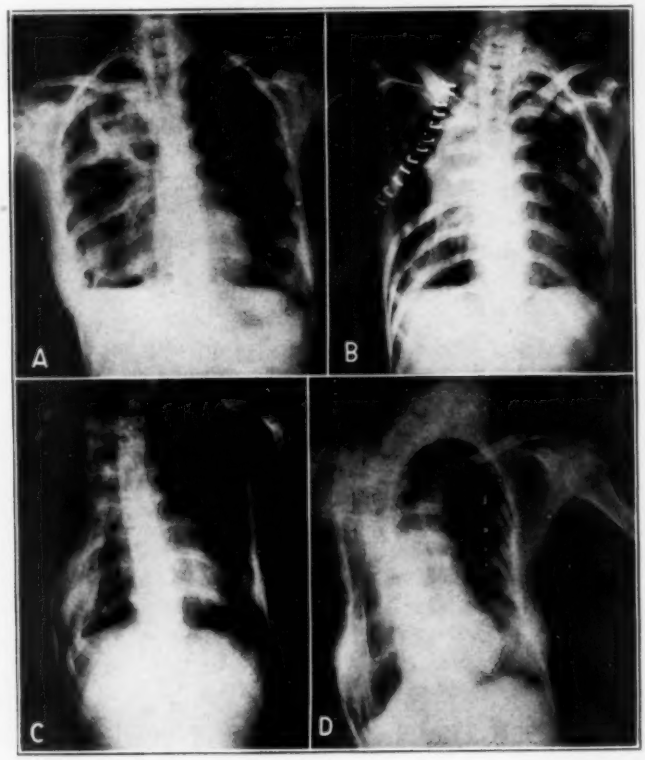

Fig. 1.—Roentgenograms of G. B.: *A*, taken before operation, shows extensive tuberculosis with cavitation in the right side of the thorax. *B*, taken in September 1935, after a two stage thoracoplasty by which six ribs were removed, shows the transverse process of the second thoracic vertebra destroyed and large stumps where the other ribs were removed. *C*, taken seven months after thoracoplasty, shows curvature of the spinal column with the deforming convexity localized at the third thoracic vertebra. *D*, taken in June 1940, after two more ribs were resected, revision performed and more transverse processes removed, reveals that the curve of the spinal column has been aggravated.

4. Bisgard, J. D.: Thoracogenic Scoliosis: Influence of Thoracic Disease and Thoracic Operations on Spine, Arch. Surg. **29**:417-445 (Sept.) 1934.

some conclusions which must be considered as extremely important to the orthopedic surgeon.

His principal observations were that a convexity occurred toward the side on which the operation was performed and that this convexity depended on three factors: (1) the number and the length of the dorsal segments resected; (2) the site of the rib resection, because the higher the area of the operation, the greater the effect on the

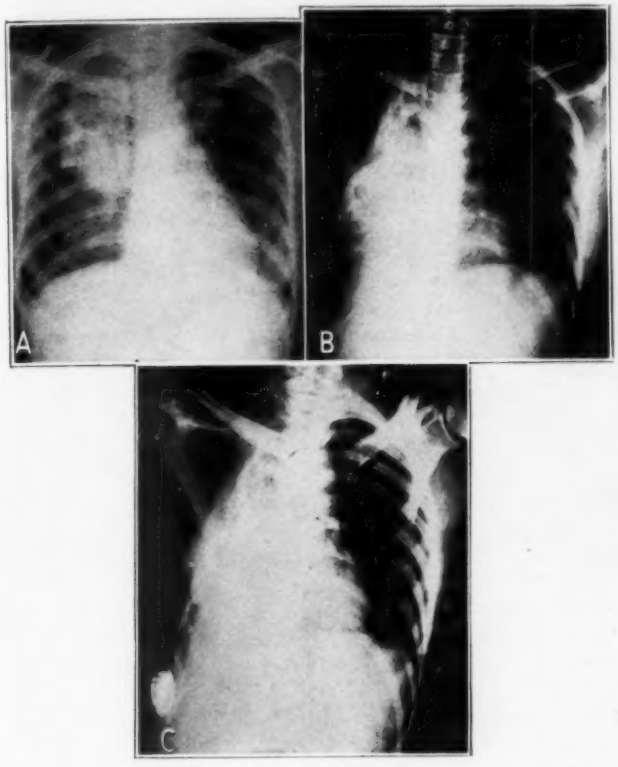

Fig. 2.—Roentgenograms of E. B.: *A*, taken in January 1938, shortly before operation, discloses marked tuberculosis in the right side of the thorax but no deviation of the spinal column. *B*, taken after extensive thoracoplasty, shows the transverse processes intact and no deviation of the spinal column. *C*, taken a few months later, demonstrates that scoliosis is still absent in spite of the operation.

curvature, and (3) the relative position of the resected rib to the spine, because the greater the proximity, the greater the effect on the curvature.

The thoracic explanations which Bisgard offered to clarify the phenomena were not entirely correct and were somewhat confusing. However, much credit must be given to him for his general observations,

because these made orthopedic surgeons look with interest on the possibility of using the procedure in the treatment of scoliosis.

The present study was made with these facts in mind. All the available material at Sea View Hospital was reviewed. There were some insurmountable obstacles. Roentgenograms are kept for only five years unless the patient is still being treated at the end of that time. In many cases the roentgenograms were not taken with a Bucky diaphragm, and the spine showed up so poorly that the material was unsatisfactory for analysis. However, in spite of these handicaps, it was possible to collect 256 cases in which rib resection had been performed. Cases in which the extensive Shede operation had been performed were intentionally omitted, as this operation is not applicable to the treatment of scoliosis.

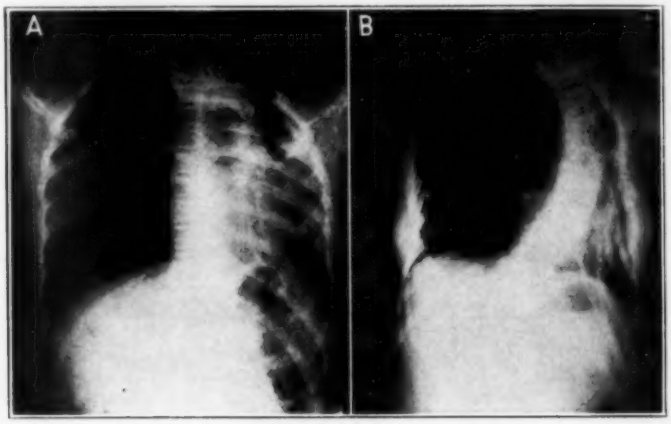

Fig. 3.—Roentgenograms of G. C. (the case of this patient was reported some years ago by Dr. M. Cleveland): *A*, taken after an unsuccessful attempt at artificial pneumothorax, shows extensive tuberculosis in the left side of the thorax. *B* was made after extensive resection by which eleven ribs were removed; the only transverse processes left intact are those of the first, second and third thoracic vertebrae; marked scoliosis is present.

Every effort was made to limit the study to those patients who underwent only rib resection.

A survey of all the roentgenograms of patients on whom thoracoplasty had been done was made with the idea of determining the cause of the characteristic scoliosis in these patients. The study was undertaken for the purpose of possibly using the essential parts of the operation to treat primary scoliosis.

The total number of cases in which resection was performed was 256; 140 of the patients were men, 107 were women, and 9 were children. Before operation 30 of the patients had scoliosis. Postoperative scoliosis

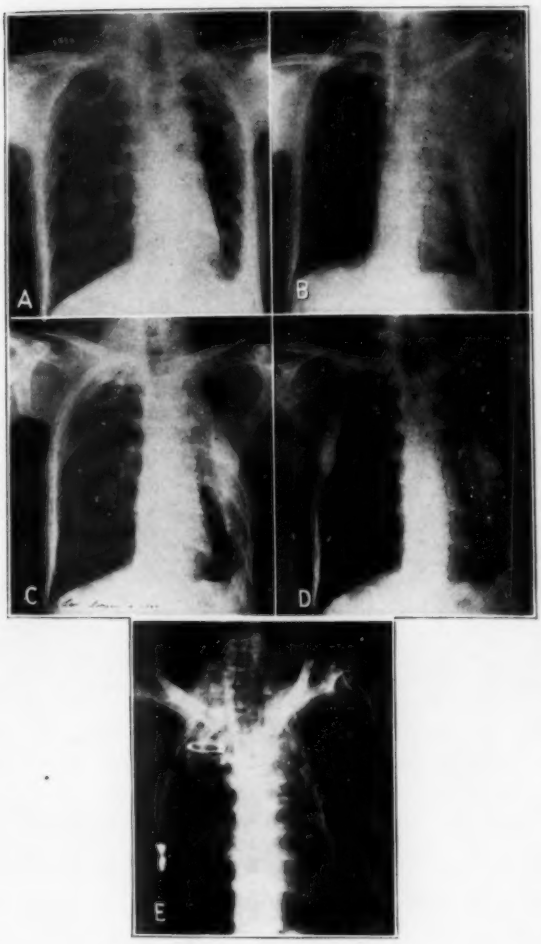

Fig. 4.—Roentgenograms of L. D.: *A*, taken before operation, reveals far advanced tuberculosis with excavation in the upper portions of the fields of both lungs; the spine is straight. *B*, made after a two stage thoracoplasty by which the upper seven ribs were removed from the left side, shows the transverse processes intact and short sections of the ribs remaining. *C*, taken after a one stage thoracoplasty by which the upper three ribs were removed from the right side, shows the transverse processes left intact. *D*, taken after a second stage thoracoplasty by which two more of the upper ribs were removed from the right side, shows the transverse processes intact and no scoliosis. *E*, made after a third stage thoracoplasty by which one more rib was removed from the right side (this made a total of seven ribs removed from the left and six from the right side), shows all transverse processes intact and the spinal column still straight.

with a shift of the deforming convexity to the side opposite that on which resection had been done or with overcorrection affected 11 men and 9 women. The relation of scoliosis to the type of operation and the number of ribs resected is shown in the table. In the 140 cases in which the patients were men, there was a shift of the spinal column to the right after rib resection in 55, a shift to the left in 67 and no shift at all in 18. In the 107 cases in which the patients were women there was a shift of the spinal column to the right after rib resection in 48, a shift to the left in 40 and no shift at all in 19.

It has been pointed out on numerous occasions that scoliosis after intrathoracic pathologic change is of two main types. In the first type

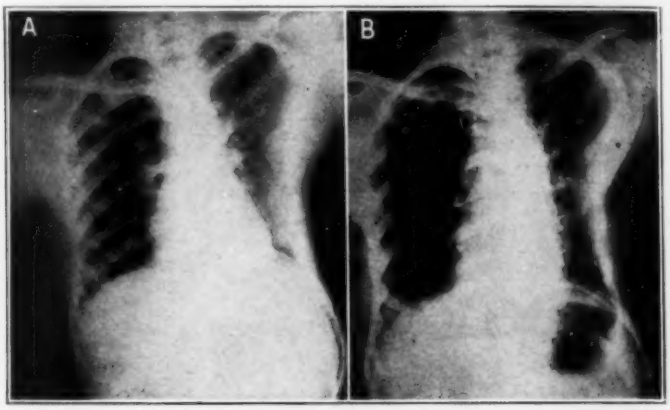

Fig. 5.—Roentgenograms of M. S. H.: *A*, taken on admission, shows evidence of a basal thoracoplasty performed elsewhere and practically no deviation of the spinal column. *B*, taken after more extensive thoracoplasty, shows the transverse processes intact and only a little deviation of the spinal column.

Relation of Scoliosis to the Stage of Resection and the Number of Ribs Resected

Stage of Resection	Ribs Resected in Men with Scoliosis		Ribs Resected in Men Without Scoliosis		Ribs Resected in Women with Scoliosis		Ribs Resected in Women Without Scoliosis	
	Right	Left	Right	Left	Right	Left	Right	Left
First	7	6	5	6	5	4	5	6
Second	19	32	3	4	18	20	4	0
Third	29	29	0	0	25	16	2	2
Total	55	67	8	10	48	40	11	8

there is concavity to the diseased side, such as occurs with pleural or pulmonary diseases in which the chronic inflammatory processes result in extensive scar tissue contraction. The second type is scoliosis after

thoracoplasty. In the latter there is always convexity to the side on which operation has been performed.

One readily understands, then, that a patient with a chronic disease of the lungs has a scoliotic deformity to one side and that after thoracoplasty the spine shifts with the convexity to the opposite side. The questions naturally arise: What element causes this shift? Can this

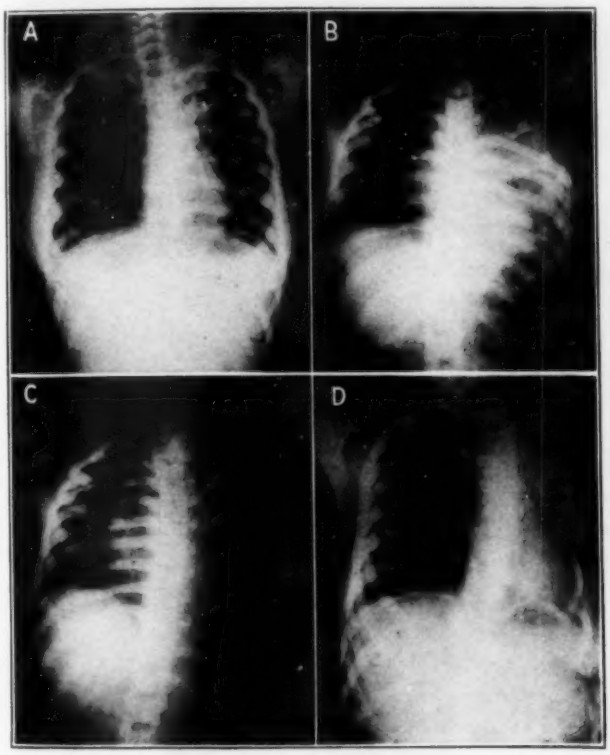

Fig. 6.—Roentgenograms of E. L.: *A*, made in February 1933, shows far advanced caseous pneumonic disease with a large excavation in the upper two thirds of the field of the left lung; there is a slight, gentle C curve in the spinal column, which is probably a postural condition. *B*, taken in 1933, after a one stage thoracoplasty by which the upper four ribs were removed, demonstrates that the transverse processes of the third and fourth thoracic vertebrae have been partially destroyed and that there is little change in the contour of the spinal column. *C*, taken six months later, after a more complete thoracoplasty by which the upper ten ribs were removed, shows that the transverse processes from the third to the tenth thoracic vertebrae have either been destroyed or removed and that there is a C curve in the spinal column with its apex at the level of the fifth thoracic vertebra which shows greater curvature than the original postural defect. *D*, taken four months later, shows little change in the curvature of the spinal column and considerable regeneration of the ribs along the spinal column.

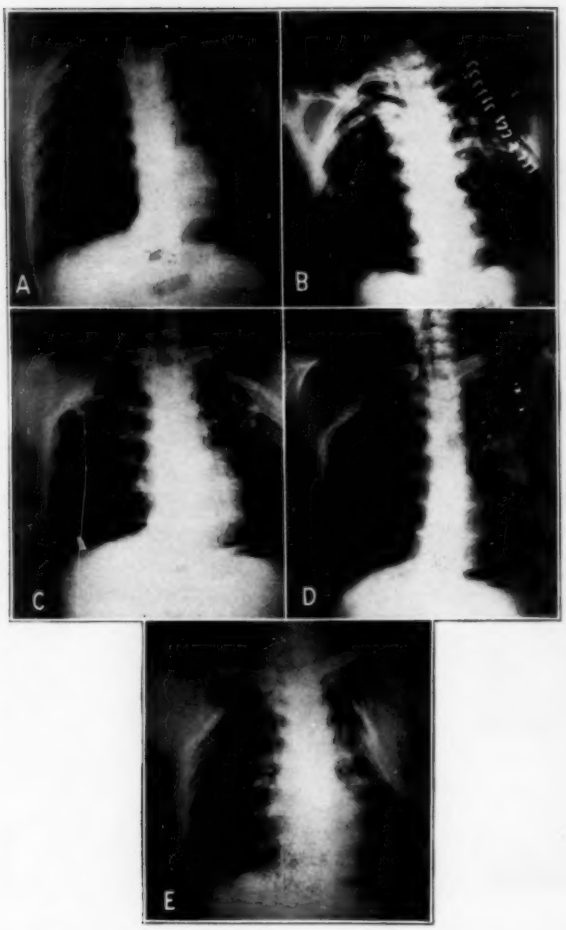

Fig. 7.—Roentgenograms of I. S.: *A*, taken in June 1936, shows far advanced caseous pneumonic disease with numerous cavities in the upper half of the fields of both lungs and the spinal column straight. *B*, taken in November 1936, after a one stage thoracoplasty by which the upper four ribs were removed from the left side, shows the transverse processes intact. *C*, made on June 3, 1937, after a one stage thoracoplasty by which four ribs were removed from the right side, shows the transverse processes intact and the spinal column straight. *D*, made on June 23, 1937, after a second stage thoracoplasty by which three more ribs were removed from the left side, shows the transverse processes intact, large segments of the ribs visible and the spinal column straight. *E*, made in March 1940, after a bilateral thoracoplasty by which seven ribs were removed from the left side and four from the right, shows the transverse processes intact and the spinal column straight.

element be determined in advance? How many ribs must be resected and where must this resection take place?

Analysis shows the following facts:

1. In the majority of the cases there was convexity of the spine toward the operative side.

2. The number and the length of the costal segments resected do not of themselves alter the resulting scoliosis.

3. In all cases in which there was marked convexity to the side on which operation had been performed either the transverse process was injured or the anterior costotransverse ligament was cut. In cases in which the transverse processes were left intact, slight curvature or none at all resulted.

4. In all the cases (3.5 per cent) in which the patients were children there was destruction of the transverse processes. This possibility explains the severe postoperative curvature.

5. Resecting a larger number of ribs does not necessarily increase the curvature. However, if a transverse process is injured or removed the curvature occurs.

6. Resection lateral to the angles of the ribs causes practically no deviation except in children.

7. There are no sharply angulated curves; that is, there are no wedged vertebrae. (All are C curves.)

8. As successive rib resections are carried out at lower levels, the apex of the curve descends.

9. Mediastinal displacement does not necessarily cause scoliosis.

10. There was no change in spinal curvature in 7 cases in which basal thoracoplasty was performed. Apparently basal thoracoplasty has little effect on the spine.

11. In cases in which successive ribs are removed and at one point a transverse process is resected, the apex of curve suddenly localizes at that point, and the curve increases.

12. Regeneration of ribs will prevent scoliosis.

13. In all cases the resulting curve averaged 18 degrees.

To the orthopedic surgeon the foregoing analysis is especially significant. The question naturally occurs: Can a similar procedure be carried out in order to correct preexisting true scoliosis? There is evidence that this use of the procedure is worth investigating; in fact, it has already been attempted. These studies favor strongly the opinion that the essential element is not the rib but the transverse process.

An attempt at explanation of the observed phenomena is intentionally avoided. The pathologic physiology of this condition has as

yet not been adequately expounded. Such explanations as have been given are hypothetic.

CONCLUSION

The main conclusions of this study are that scoliosis resulting from thoracoplasty is due to trauma or removal of the transverse processes and that the rib resection of itself has little if any influence in causing the condition. On the basis of these findings transversectomy to correct primary scoliosis is now being done on the concave side of the spinal curvature.

CAPILLARY PERMEABILITY AND INFLAMMATION IN RABBITS WITH STAPHYLOCOCCIC SEPTICEMIA

AN EXPERIMENTAL STUDY

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Capillary permeability and inflammation have been studied recently in the rabbit under varying experimental conditions. Observations on the localization and the concentration of intravenously injected trypan blue in the skin of the normal animal have shown that this dye localizes and concentrates only during a specific interval following the local application of xylene.[1] This interval is not determined by either the presence or the absence of edema and hyperemia. Furthermore, the time in which the greatest number of leukocytes localize in the xylene-treated areas of the skin follows by several hours the localization and the concentration of the dye.[1b]

Materials such as vaccine virus, india ink, antitoxin and staphylococci when given intravenously localize and concentrate in areas of inflammation in a manner similar to that of trypan blue.[2] Both capillary permeability and the localization of leukocytes in areas of injury are affected by alcohol, by certain anesthetics and by epinephrine.[3] Pickrell [3a] found that alcoholic intoxication maintained at the point of stupor destroys the resistance of the rabbit to pneumococcic infection. According to Pickrell, this loss of resistance "appears to be due to the fact that intoxication profoundly inhibits the vascular inflammatory response as long as

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This study was aided by grants from the John and Mary R. Markle Foundation and from the University of Tennessee.

1. Rigdon, R. H.: (*a*) Capillary Permeability in Areas of Inflammation Produced by Xylene, Arch. Surg. **41**:101 (July) 1940; (*b*) Relation of Capillary Permeability to Inflammation, South. M. J. **34**:292, 1941.

2. Rigdon, R. H.: Localization of Staphylococcus Antitoxin in Areas of Inflammation, J. Lab. & Clin. Med., to be published; footnote 1.

3. (*a*) Pickrell, K. L.: The Effect of Alcoholic Intoxication and Ether Anesthesia on Resistance to Pneumococcal Infection, Bull. Johns Hopkins Hosp. **63**:238, 1938. (*b*) Cressman, R. D., and Rigdon, R. H.: Capillary Permeability and Inflammation in Narcotized Rabbits, Arch. Surg. **39**:586 (Oct.) 1939. (*c*) Rigdon, R. H.: A Study of Capillary Permeability and Inflammation in the Skin of Rabbits Given Adrenalin, Surgery **8**:839, 1940.

the intoxication is maintained . . ." Leukocytes fail to emigrate to the bacteria. Cressman and Rigdon [3b] observed that "capillary permeability in areas of inflammation is altered in rabbits narcotized with alcohol or ether, as demonstrated by the localization and concentration of trypan blue."

Epinephrine given either intradermally or intravenously in large quantities inhibits the development of hyperemia in the areas of the skin to which xylene has been applied. The number of polymorphonuclear leukocytes is decreased around staphylococci when epinephrine is injected intradermally. "The failure of leucocytes to reach an area infiltrated with staphylococci when the animal is given large quantities of adrenalin either intradermally or intravenously apparently may be the result of vascular constriction." [3c]

In a group of rabbits given staphylococci intravenously polymorphonuclear leukocytes failed to localize in the xylene-treated areas of the skin.[4] This observation appears significant, since the absence of leukocytes may be due either to a diminution in the number of white blood cells in the circulating blood or to some local vascular or tissue change. This paper presents a further study of capillary permeability and inflammation in the skin of rabbits with staphylococcic septicemia.

CAPILLARY PERMEABILITY IN THE SKIN OF RABBITS AFTER THE INTRAVENOUS INJECTION OF STAPHYLOCOCCI

The technic used in this experiment for the study of capillary permeability is the same as that used in earlier investigations.[5] The skin over the sides and the abdomen of the rabbit is carefully shaved twenty-four hours or more before the experiment is begun. Xylene is carefully applied with a cotton applicator to local areas of the skin at varying intervals before 10 cc. of a 0.2 per cent solution of trypan blue is given intravenously.

The skin in the normal adult rabbit becomes hyperemic thirty to sixty seconds after the local application of xylene. Edema also quickly appears. The macroscopic evidence of inflammation usually persists for four or five days. Intravenously injected trypan blue localizes and concentrates in the xylene-treated areas only during a specific interval.[1] Essentially the same amount of dye concentrates in xylene-treated areas as in the untreated areas of the skin when the irritant is applied three hours or longer before the dye is given. The largest amount of dye localizes and concentrates in the xylene-treated area when the irritant is applied immediately before the dye is injected. There is a progressive diminution in the quantity of dye that localizes and concentrates in xylene-treated areas when the interval between the application of the irritant and the intravenous injection of the dye is progressively increased.

Sixteen rabbits with staphylococcic septicemia were used to study the localization and the concentration of trypan blue in xylene-treated areas of the skin.

4. Rigdon, R. H.: Localization of Staphylococci in Areas of Inflammation Produced by Xylene, Arch. Surg. **41**:879 (Oct.) 1940.

5. Rigdon (footnotes 1 *a*, 3 *c* and 4). Cressman and Rigdon.[3b]

The animals were given 10 cc. of a heavy suspension of staphylococci in a solution of sodium chloride. Xylene was applied, and trypan blue was given to 7 of these rabbits within two hours after the injection of the bacteria. The macroscopic reaction, the time of reaction and the quantity of dye that localized and concentrated in the skin were the same as with normal adult rabbits.

In 9 rabbits xylene was applied from three to eight hours after staphylococci were injected. This delay in the application of xylene was made to see whether animals sick with staphylococcic septicemia reacted the same as normal rabbits. The general appearance of these 9 rabbits varied widely at the time the xylene was applied. Hyperemia and edema occurred in some of these rabbits after the application of xylene, exactly as it does in normal animals. In some rabbits, however, there was either a diminution or a complete absence of hyperemia after the application of xylene. The case of rabbit 739 illustrates the failure of hyperemia to occur:

9:30 a. m. 10 cc. of a suspension of staphylococci in a solution of sodium chloride given intravenously.

5:30 p. m. Xylene applied to area 1.

5:45 p. m. Xylene applied to area 2; the rabbit was sick and too weak to stand.

6:00 p. m. Xylene applied to area 3.

6:15 p. m. Xylene applied to area 4; there was no hyperemia or edema in the xylene-treated areas.

6:15 p. m. 10 cc. of trypan blue given intravenously; the rabbit died.

There was also a variation in the time of reaction and in the quantity of trypan blue that localized and concentrated in the xylene-treated areas of the skin in the rabbits which were sick after the injection of staphylococci. The case of rabbit 740 illustrates the failure of trypan blue to localize and concentrate in xylene-treated areas:

9:30 a. m. 10 cc. of a suspension of staphylococci in a solution of sodium chloride given intravenously.

5:30 p. m. Xylene applied to area 1.

5:45 p. m. Xylene applied to area 2.

6:00 p. m. Xylene applied to area 3.

6:05 p. m. The skin was hyperemic in areas to which xylene had been applied.

6:15 p. m. Xylene applied to area 4; 10 cc. of trypan blue given intravenously.

6:25 p. m. No dye in any of the xylene-treated areas.

6:27 p. m. The rabbit was too weak to stand.

6:40 p. m. A reddish brown color was present in the areas of the skin treated with xylene.

6:37 p. m. Rabbit died; no dye localized in any of the xylene-treated areas.

It was difficult to control this experiment since the reaction to the inoculation of staphylococci varied in the different rabbits. It may be concluded from these experiments, however, that the skin reaction to xylene and the localization

of trypan blue in xylene-treated areas in the animals given staphylococci vary from those in normal adult rabbits.

LOCAL INFLAMMATORY REACTION IN THE SKIN OF RABBITS WITH STAPHYLOCOCCIC SEPTICEMIA

Eighteen rabbits were used. Xylene was carefully applied with a cotton applicator to small areas of skin at intervals of six, four and two hours before the

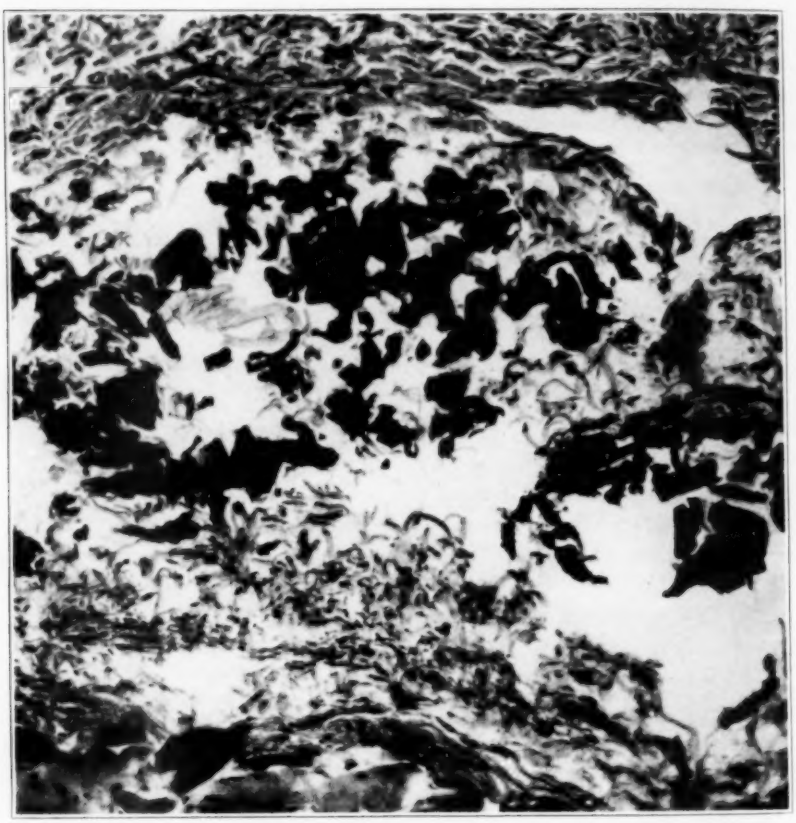

Fig. 1.—This rabbit (332) was given 10 cc. of a heavy suspension of staphylococci in a solution of sodium chloride intravenously and, immediately thereafter, 0.2 cc. of a 2 per cent suspension of aleuronat intradermally. It was killed six hours later. There were no leukocytes infiltrating the particles of aleuronat.

animals were killed. Two tenths of a cubic centimeter of a heavy suspension of staphylococci in a solution of sodium chloride and a similar amount of a 2 per cent suspension of aleuronat in a solution of sodium chloride were injected intradermally in different areas at the same time that xylene was applied. The bacteria had been grown on the surface of infusion agar and had been washed and suspended in a solution of sodium chloride.

Five of the rabbits were given 10 cc. of a heavy suspension of staphylococci in a solution of sodium chloride intravenously at the beginning of the experiments. There was marked diminution of hyperemia where xylene was applied and bacteria and aleuronat were injected intradermally. In 4 of the rabbits given staphylococci intravenously there were essentially no leukocytes in either the areas of the skin where xylene was applied or around the particles of aleuronat and the bacteria. There were only a few leukocytes about the irritants in 1 of the rabbits in this group. In the 13 control animals there were many leukocytes in the area to

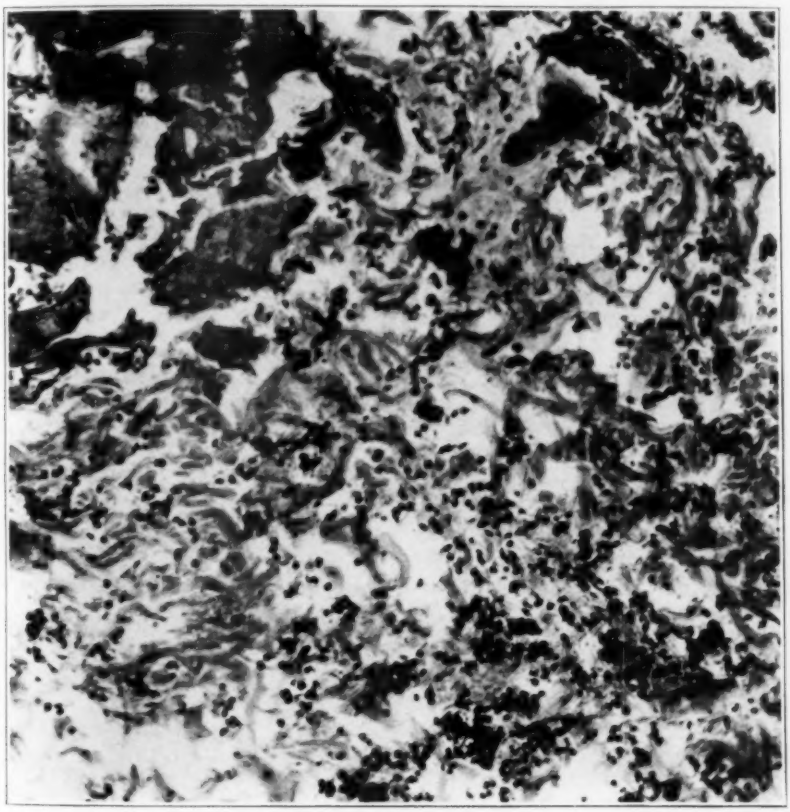

Fig. 2.—This rabbit (337) served as a control for 332. Aleuronat was injected. There were many leukocytes infiltrating the tissues around the particles of aleuronat.

which xylene was applied and in which staphylococci and aleuronat were injected (figs. 1 and 2).

A second group of 7 rabbits were given a similar quantity of aleuronat and a corresponding number of staphylococci intradermally. The injections were made at intervals of six, four and two hours before the rabbits were killed. Five of the rabbits were given intravenously 10 cc. of a heavy suspension of staphylo-

cocci in a solution of sodium chloride. Three of these rabbits did not show any leukocytes about the staphylococci and aleuronat, while 1 animal had only a few cells. The fifth rabbit had essentially the same number of leukocytes as the 2 control animals (fig. 3).

A third group of 7 rabbits were given intradermal injections of 0.2 cc. of a heavy suspension of staphylococci in a solution of sodium chloride. At the same time they were given 10 cc. of the same suspension intravenously. These rabbits

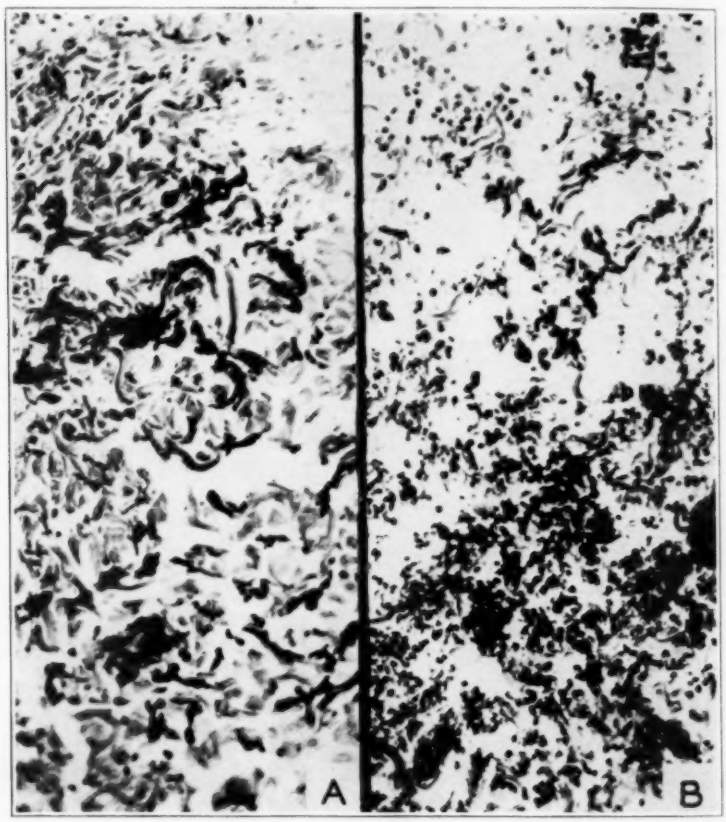

Fig. 3.—*A*, this rabbit (328) was given 10 cc. of a heavy suspension of staphylococci in a solution of sodium chloride intravenously and, immediately thereafter, 0.2 cc. more intradermally. It was killed six hours later. There were no leukocytes infiltrating the tissues around the groups of bacteria. *B*, this rabbit (337) served as a control for 328. Many leukocytes were infiltrating the tissue into which the bacteria had been injected.

were killed two hours later. No leukocytes were present in the tissues about the bacteria.

It is evident from these observations that polymorphonuclear leukocytes do not localize and concentrate around staphylococci and aleuronat and in the corium

in the areas to which xylene is applied when rabbits are given 10 cc. of a heavy suspension of staphylococci in a solution of sodium chloride intravenously before the application or the injection of the irritants.

TOTAL NUMBER OF WHITE BLOOD CELLS IN THE CIRCULATING BLOOD AFTER THE INTRAVENOUS INJECTION OF STAPHYLOCOCCI

The observations in the preceding experiment showed that polymorphonuclear leukocytes fail to localize and to concentrate about staphylococci and aleuronat when they are injected intradermally into rabbits previously given a heavy suspension of staphylococci in a solution of sodium chloride intravenously. In view

White Blood Cells in the Peripheral Blood of Rabbits Given Staphylococci Intravenously

Rabbit	Control Average Number of White Blood Cells	Time Staphylococci Were Given Intravenously	Time and Number of White Blood Cells in Peripheral Blood						Death	
			10 a.m.	11 a.m.	12 m.	1 p.m.	2 p.m.	3 p.m.	Time	Manner
482	8,800	9:05 a.m.	15,650	2,050	3,800	4,750	1,850	3,750	3:45 p.m.	Died
484	8,462	9:05 a.m.	13,750	.....	.....	.....	.....	.....	10:45 a.m.	Died
485	7,750	9:05 a.m.	3,750	2,000	3,550	3,050	.....	.....	1:30 p.m.	Died
486	9,725	9:05 a.m.	15,500	6,750	11,050	5,400	.....	.....	1:30 p.m.	Died
487*	7,025	10:00 a.m.	.....	2,800	.....	1,900	.....	.....	1:30 p.m.	Killed
488*	6,700	10:00 a.m.	.....	40,800	.....	3,650	.....	.....	1:30 p.m.	Killed
490*	6,625	10:00 a.m.	.....	3,100	.....	2,100	.....	.....	1:30 p.m.	Killed
491*	6,425	10:00 a.m.	.....	4,000	.....	2,750	.....	.....	1:30 p.m.	Killed
492*	7,327	10:00 a.m.	.....	3,250	.....	5,400	.....	.....	1:30 p.m.	Killed

* These rabbits were given an intradermal injection of 0.2 cc. of the suspension of staphylococci at 11:30 a. m. No leukocytes were present about the staphylococci in the skin in any of these rabbits. Xylene was applied to an area of the skin of each of these rabbits, and 10 cc. of trypan blue was given intravenously to make possible a study of capillary permeability. The dye localized the saline in the xylene treated areas as it does in normal rabbits.

of this observation the number of leukocytes in the circulating blood of similarly treated rabbits was studied.

Standard technic was used in obtaining and counting the white blood cells. Blood was obtained from the ears. The interval between the injection of the bacteria and the time the blood was taken for the counts is shown in the table. The data were obtained from a group of 9 adult rabbits given a heavy suspension of staphylococci intravenously. Leukopenia developed in these rabbits within an hour.

The following experiment was made to determine the effect of various dilutions of staphylococci on the number of white blood cells. A suspension of staphylococci in a solution of sodium chloride was injected into 4 rabbits intravenously, and the leukocytes were counted. The same volume of a suspension of staphylococci in a solution of sodium chloride, in which, however, the number of bacteria represented a 1 to 3 dilution, was injected intravenously into a second group of 4 rabbits. The result of this experiment is shown in figure 4. The

number of circulating leukocytes in this experiment was apparently influenced by the number of staphylococci injected. Death occurred more quickly in the group given the heavy suspension than in the group given the lighter inoculum. The staphylococci apparently multiplied after injection, and accompanying this multiplication there occurred leukopenia, as shown in figure 4. When the heavy suspension was used, leukopenia occurred immediately and persisted until death. When a light suspension was injected, leukocytosis was sometimes followed by leukopenia which persisted until death.

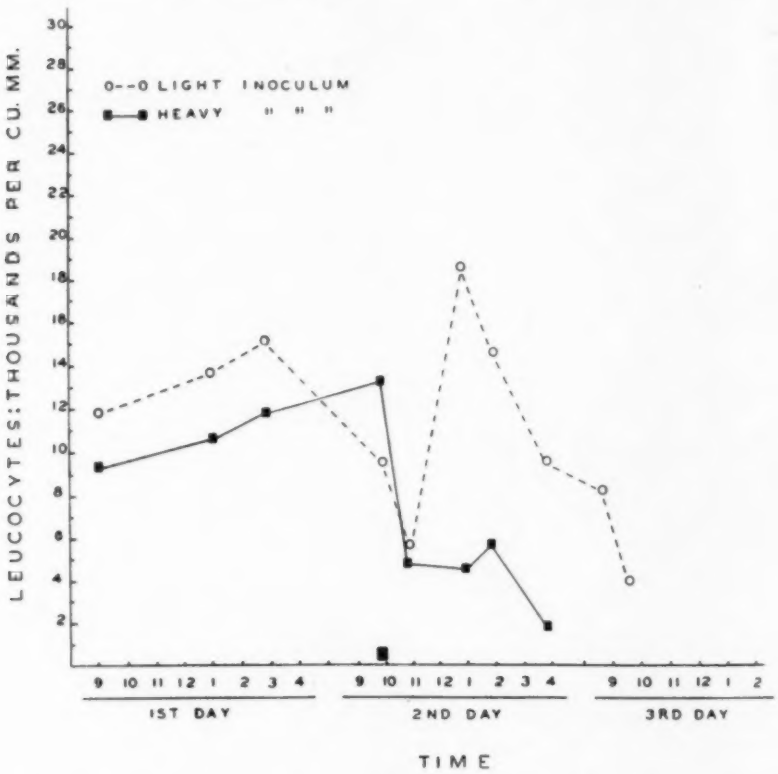

Fig. 4.—The white blood cell count in 8 rabbits (4 in each group) given 10 cc. of a suspension of staphylococci in a solution of sodium chloride intravenously. The light inoculum represents a dilution of 1 to 3 of the heavy inoculum. All rabbits given the latter were dead by 5 p. m. Those given the light inoculum survived for a longer period. However, all were dead twenty-eight hours after the injection of the bacteria.

COMMENT

These experiments show that both the macroscopic and the microscopic reactions in the skin of rabbits sick with staphylococcic septicemia vary from those in the skin of the normal rabbit. The reactions of the rabbits sick with staphylococcic septicemia are similar to those of animals given

alcohol and ether and resemble the reactions that may occur in rabbits given large injections of epinephrine.[3]

The vascular response to an irritant may be completely absent in the skin of the rabbit with staphylococcic septicemia. This vascular phenomenon may be associated with the fall in the blood pressure which may accompany septicemia. Blalock,[6] in discussing acute circulatory failure, stated that "many different factors may enter into the production of shock that is associated with operations. Among these may be included hemorrhage, infection, anaesthesia, and particularly the disease for which the operation is performed."

The absence of polymorphonuclear leukocytes around the staphylococci and the particles of aleuronat in the skin of rabbits suggests the possibility either that there is a deficiency in the number of leukocytes in the circulating blood or that some inhibitory process has occurred to prevent the localization of these cells in the area of the irritants. The observations made in this study as well as those of Ewing[7] indicate that leukopenia may follow the intravenous injection of staphylococci in the rabbit. It would seem from this study, however, that there are a sufficient number of white blood cells in the blood for at least a few to localize around the staphylococci in the skin. It appears more likely that the circulation in the small blood vessels in the skin is either diminished or completely absent in rabbits with severe staphylococcic septicemia. This appears likely in view of the complete absence of white blood cells around the staphylococci and the particles of aleuronat and the failure of trypan blue to localize and concentrate in xylene-treated areas of the skin. The leukocytes are inhibited from reaching the site of injury by the presence of this vascular constriction. In the study of capillary permeability and inflammation in rabbits given epinephrine it was suggested that the inhibition in the development of inflammation may be accounted for by vascular constriction.[3e]

It will be shown in subsequent publications that a similar inhibition in the development of an inflammatory reaction may accompany loss of blood by bleeding and also severance of the spinal cord in the adult rabbit.

The results obtained in this study show that a small number of staphylococci injected intravenously may cause leukopenia which is followed by leukocytosis. After this leukocytosis there occurs leukopenia which persists until death. Certain bacteria may fail to produce any change in the number of leukocytes; the number of bacteria, their virulence and the resistance of the host must be remembered.

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6. Blalock, A.: Acute Circulatory Failure as Exemplified by Shock and Hemorrhage, Surg., Gynec. & Obst. **58**:551, 1934.

7. Ewing, J.: Toxic Hypolencocytosis, New York M. J. **61**:257, 1895.

SUMMARY

Capillary permeability and inflammation as observed in the skin of the rabbit after the injection of trypan blue vary in the animal with staphylococcic septicemia as compared with the normal rabbit. This variation apparently may be associated with constriction of the small blood vessels in the skin.

The reaction to xylene, staphylococci and aleuronat in rabbits with staphylococcic septicemia is similar to that which may occur in rabbits anesthetized with alcohol or ether or given large quantities of epinephrine.

REDUCED TEMPERATURES IN SURGERY

II. AMPUTATIONS FOR PERIPHERAL VASCULAR DISEASE

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One of us (F.M.A.) [1] has suggested possible surgical uses of cold on the evidence of animal experiments and a few clinical cases. Since the adoption of this method as a routine in City Hospital, sufficient clinical evidence has been accumulated to permit an evaluation of the results. This paper gives (1) the reports of 9 cases, in which fatalities, partial successes or difficulties encountered in the early experience are represented, and (2) a table of the results in the entire series of 45 cases to date. The majority of the cases belong to the initial period in which ice or ice water was used for chilling. In the later cases a special refrigerating apparatus has been used in the preparation of patients for operation, producing the same effect more conveniently.

REPORT OF CASES

CASE 1.—A Russian Jewish peddler aged 82 years was admitted Jan. 8, 1941 with arteriosclerosis. The general history was noncontributory, and he had used no alcohol or tobacco. For one year he had been unable to stand for any length of time because of pain in both feet. The pain increased, and discoloration began a short time before admission. The salient observations in the examination were as follows: The temperature was 100.2 F. The blood pressure was 115 systolic and 80 diastolic. The urine and the chemical composition of the blood were normal. There was atrophy of the tissues of both legs from the knees down and black gangrene of all the toes of both feet. Pulsation was absent in the popliteal arteries and everywhere below. There was coldness to touch beginning at the middle

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From the Surgical Division, City Hospital.

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1. Allen, F. M.: (*a*) Local Asphyxia and Temperature Changes in Relation to Gangrene and Other Surgical Problems, Tr. A. Am. Physicians **52**:189, 1937; (*b*) Reduced Temperatures in Surgery: I. Surgery of Limbs, Am. J. Surg. **52**: 225, 1941.

of the dorsum of the right foot and about the middle of the left calf; in the left leg there were dusky red streaks from the gangrenous area up to the knee.

Operation was advised but refused until January 12, when the entire left foot was dark colored; the streaks of lymphangitis extended above the knee joint, and the temperature was 102 F. The leukocyte count was 22,000 with 81 per cent polymorphonuclears and 30 per cent young forms.

Prior to operation on January 12, ⅙ grain (0.01 Gm.) of morphine sulfate and 1/150 grain (0.0004 Gm.) of scopolamine hydrobromide was given hypodermically because of the patient's apprehension and nervousness but had no visible effect. A tourniquet consisting of two turns of pure gum tubing was applied a little below the middle of the left thigh, tightly enough to stop the arterial flow. The head of the bed was elevated; the leg was placed on a layer of cracked ice in a rubber sheet and then completely buried in ice up to several inches above the tourniquet. The melting ice drained into a bucket beside the bed. The patient, with the ice still on his leg, was carried to the operating room in time to start the operation two hours after the beginning of refrigeration. He was placed on the operating table without ice, and the operative field was painted with tincture of zephiran.[2] The procedure was an amputation through the lower part of the thigh after a method to be described later. No drainage was used.

The patient had eaten a regular meal before the operation and experienced no discomfort. The blood pressure ranged from 105 systolic and 80 diastolic before the operation to 130 systolic and 90 diastolic during the operation and at the end. The pulse and respiration rates did not change.

The wound was lightly dressed, and ice bags were applied continuously. No signs of shock were seen in the subsequent condition or behavior of the patient. By the next day the temperature had fallen to 99.5 F. On the second day there was a return of fever, complaints of dyspnea and suggestive signs in the lung; all of these cleared up after the administration of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole). On the seventh day after operation the sutures were removed, and about 25 cc of odorless discharge was expressed from one angle of the wound.

During the days immediately following the operation a dark violet discoloration extended rapidly over the right foot. Consent for a second amputation was not obtained; ice bags were therefore used continuously to keep this foot at almost ice temperature. The spread of gangrene and infection was thus apparently delayed, and the good general condition indicated absence of septic absorption, but there was no tendency toward healing or demarcation.

On January 21 (nine days after the first operation) the entire right foot was so dark in color that the patient accepted amputation. The methods were essentially the same as in the first operation, and the procedure resulted in primary union.

Although both stumps were seemingly in excellent condition, there were occasional moderate elevations of temperature, not to be explained by lack of response to sulfathiazole. Appetite and strength slowly failed, though the fever subsided. January 31 seemed to mark a turn for the better, with continued good condition of the wounds, a normal temperature and the return of appetite and spirits, but death occurred that night during sleep.

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2. Zephiran is alkyldimethylbenzyl-ammonium chloride. It is a cationic detergent having about the same consistency and physical properties as liquid soap, which is an anionic detergent.

The apparent lack of disturbance from two thigh amputations in a senile patient seems to illustrate the shock-saving character of the procedure. The death may reasonably be attributed to delayed shock, which has been discussed elsewhere,[1] and to the general strain of wound healing and minor degrees of lingering infection. The patient's strength might have been better preserved if earlier consent for amputation could have been obtained.

CASE 2.—A German housewife was admitted Jan. 15, 1941 with diabetic gangrene. Her age was given as 64 years, but her appearance suggested a greater age. The diabetes was of uncertain duration, but she had recently had polyuria and loss of weight. Five months before, she had stubbed her foot against a bed. All the toes turned dark; the first and fifth progressed to gangrene, while the others cleared up. The pain and the black area extended slowly, and a spot of gangrene also appeared on the heel.

Examination showed auricular fibrillation and systolic and diastolic murmurs over the entire precordium; these were attributed to rheumatic heart disease. In addition to the gangrene there was absence of pulsation in both popliteal arteries and below. Glycosuria and hyperglycemia were cleared up under treatment by the metabolic service of City Hospital (Dr. J. F. Hart). Operation was refused, while the temperature ranged from 100.6 to 102.8 F., until January 20, when reddish streaks extended up to the knee and the temperature rose to 104 F. Amputation was then finally accepted and was performed the same day.

A narrow tourniquet was applied at the midthigh, and the leg was packed in ice to a little above this level for one and three-quarters hours. The operation was similar to that performed in case 1. The refrigeration proved to be too brief for perfect anesthesia in the thigh, because a slight and delayed sensation was felt when the sciatic nerve was cut. However, there was no important discomfort. The deep tissues were closed with fine chromic gut, and the skin with silk suture, without drainage. The blood pressure ran without important change to a little above and below 90 systolic and 50 to 60 diastolic.

The dressing was limited as usual to a few layers of gauze, and three ice bags were kept around the stump. The temperature fell within twenty-four hours to 99.8 F. Eight days after operation all sutures were removed; with refrigeration, this was too early. One corner of the wound was opened slightly; pink tissue was revealed, and about 5 cc. of serous fluid escaped. Otherwise, healing was satisfactory, without edema or dark color. On the ninth day after operation the patient seemed well enough to sit up in a wheel chair, but she died suddenly of heart failure.

The amputation was borne without signs of shock or the interruption of eating and other habits in the presence of a cardiac complication which was evidently severe according to both the examination and the termination.

CASE 3.—An Italian street cleaner aged 72 years was admitted Jan. 21, 1941 with diabetic gangrene. There was a wedge-shaped area of black gangrene proximal to and including the second, third and fourth toes of the left foot and with edema of the entire foot up to the ankle. The history was vague, except that ulceration had begun in October 1940, that he had received insulin and other

treatment in another hospital but had refused amputation and signed himself out on December 8. The salient observations in the examination were as follows: There was pallor of the skin. In one eye there was a cataract, and in the other iridectomy had been done. There was moderate atrophy of the legs below the knees. The pulse was strong in both popliteal arteries, but it was not palpable in the dorsalis pedis or the posterior tibial arteries. Oscillometry confirmed these observations. The temperature was 100.5 F. The urine contained sugar (4 plus) and acetone (1 plus). The blood sugar was 236 mg. The hemoglobin content was 80 per cent. The leukocyte count was 20,000, with 85 per cent polymorphonuclears.

Fig. 1.—Ice water preparation for operation for a patient able to sit up.

Under the care of the metabolic service of City Hospital the blood sugar was made normal within twenty-four hours, and some hypoglycemic reactions were checked with dextrose. Oliguria was treated with intravenous infusions. A tourniquet was applied in the upper part of the calf and the leg placed in chopped ice to a little above this level. The operation was unexpectedly delayed and actually began after four and one-half hours of refrigeration. Amputation was performed in the lower third of the tibia. There was a slight trickle of blood from the tibial marrow in spite of the tourniquet. After the tourniquet had been removed and the bleeding points tied, it was found that the scanty soft tissues could not be closed over the bone ends without the risk of tension. Therefore both bones were sawed off again at a slightly higher level. The wound was closed

without any complaint of pain and without drainage. The systolic blood pressure ranged between 110 and 120 throughout, except for one brief elevation to 150.

After operation, ice bags were applied outside thin dressings. The temperature fell during the night to 99.5 F. and rose the following day to 104 F. A transfusion of 500 cc. of blood was given. The temperature continued high until January 25 and then subsided. Chilling of the stump was irregular. It is uncertain whether too high or too low temperatures were responsible for the formation of superficial blebs, which were followed by necrosis. When all plans had been made for reamputation, extreme intoxication developed overnight so that operation was impossible. On the eighth postoperative day (January 29) a tourniquet was applied and the leg refrigerated, but death occurred within a few hours.

There is as yet no accurate knowledge of the duration of anesthesia after removal of the tourniquet. In this instance it was sufficient for a reamputation of bones, but it may vary with the duration of the preceding refrigeration and with the existing temperature.

Continuance of ice temperature and tourniquet pressure for four and one-half hours may be suspected as contributing to the bad result through damage to tissues or blood vessels, but other experience seems to exclude this factor and to prove that much longer continuance is still safe.

Death might have been preventable by better regulation of the postoperative temperature, by the use of drainage, by a higher initial amputation or a prompter reamputation or by correction of other possible errors due to inexperience.

CASE 4.—A Negro carpenter aged 51 years was admitted Jan. 4, 1941, with arteriosclerotic gangrene. The temperature was 99.5 F., and the general condition was good. Pain in the small toe of the right foot had begun six months before and grown steadily worse, and ulceration had gradually followed. Examination showed blood pressure of 180 systolic and 100 diastolic and a moderately enlarged heart. Both legs were atrophic below the knees. No pulsations were palpable in the popliteal arteries or below. Oscillometer waves were slight in the thigh, were barely traces below the knees and were absent lower. Roentgenograms showed marked calcification, especially from the knees downward. The small toe of the right foot was black and mummifying, and there was a large black ulcer on the dorsum over the fourth and fifth metatarsal bones. The entire foot was swollen and cyanotic, but roentgenograms revealed no osteomyelitis. During ten days the condition grew worse under routine treatment, including continuous covering with a cradle containing one 10 watt electric bulb. There was extension of the black ulceration, pain, tenderness and swelling. Sleep was not obtained with morphine or other sedatives. Dusky red streaks followed the veins as high as the ankle, and the temperature showed slight elevations to 100.8 F. The patient was reluctant to accept amputation but finally consented to have the foot alone removed.

On January 14 a tourniquet was applied to the calf, and the leg was immersed in ice water to a level of a few centimeters above the tourniquet for one and three-quarters hours. Amputation was done, slightly above the ankle joint, with closure of the skin without drainage.

Before and during the operation the pulse rate ranged from 105 to 110 and the blood pressure between 145 and 160 systolic and 95 and 105 diastolic. The patient ate a comfortable meal immediately after returning to the ward. With the relief of pain, he slept for eighteen hours.

Subsequently he found the cold uncomfortable and drew his stump away from the ice bags whenever he was not watched. At the time the dressings were done, once or twice daily, the stump was found warm, edematous, cyanotic and tender, and the wound edges showed a narrow zone of dark slough. The temperature rose to 102 F., and though there were no chest signs, sulfathiazole was given. When the patient became aware of the threatening condition of the stump and was convinced by his own observations that it appeared better when cool, he

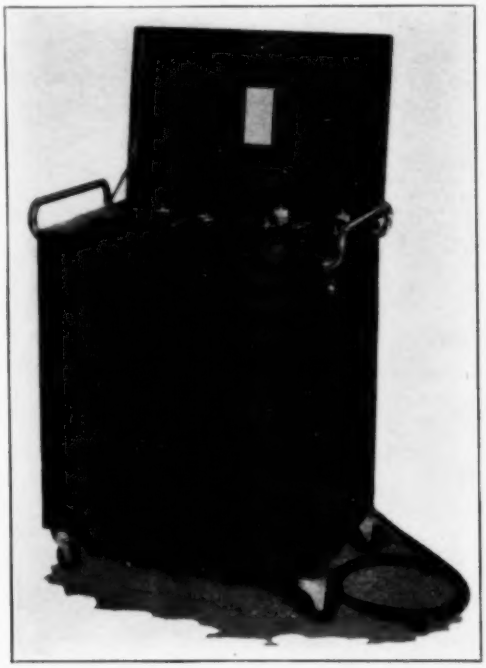

Fig. 2.—Electric unit which provides circulation for applicators which maintain any desired constant temperature about a limb.

declared that the coolness was comfortable and thereafter cooperated in retaining the ice bags. Notwithstanding improved appearances, the damage already done was sufficient to necessitate reamputation.

This amputation, between the middle and upper thirds of the tibia, was performed on February 2 by the same tourniquet-refrigeration method. Two drains of gutta-percha tissue were placed in the wound. The flaps were not full enough for the large bone, so that the tension was commented on at the time of closure. With the postoperative use of ice bags nothing more was noticeable for about a week; then a narrow zone gradually become necrotic, and all sutures were removed. This sufficed to arrest the necrosis. The temperature rose to about 102 F. without malaise. The soft tissues were left practically flush with the end of the bone

but no healing occurred. Bronchopneumonia and death seemed imminent, when amputation through the lower part of the thigh was accepted and followed by primary union.

Refrigeration seems to favor healing with a low amputation. There was a psychologic advantage in that operation was accepted sooner than if the patient had been confronted with a thigh amputation. There was a physical advantage in that repeated operations could be performed without any apparent disturbance of the patient's feelings or habits.

CASE 5.—A German janitor aged 68 years was admitted on Jan. 2, 1941 with diabetic gangrene. The temperature was normal, and the general condition was good. Fifteen years earlier he had lost the nail of the great toe of his right foot because of a blow on it, and in the course of treatment he was told that he had severe diabetes. He was given a diet and insulin but abandoned them as soon as the toe was well. His condition then ran the usual course of mild diabetes, with good nutrition and feelings, a familiar prelude to complications. Two years before admission to City Hospital he was in a hospital because of weakness; again a diet and insulin were prescribed, but he again discarded them on discharge and continued to keep good weight and apparent health. Three months before admission a painful ulcer developed on the sole of his left foot and gradually enlarged. For the past two months he had been taking 15 units of insulin, twice daily. With this he felt well, but the sugar was not controlled, and the ulcer continued to progress.

Examination showed bilateral cataracts and marked arteriosclerosis, with good nutrition and blood pressure 120 systolic and 60 diastolic. The legs were atrophic below the knees. Oscillometric waves were only slightly reduced below both knees but were small above the left ankle and absent above the right ankle. The left foot, however, had a deep painful ulcer in the metatarsal region of the sole, and there was a corresponding purplish discoloration on the dorsum.

Hyperglycemia and glycosuria (4 plus) were present without acetone. The diabetic condition was treated in the metabolic service of the City Hospital; it was controlled with a diet and an increase of insulin to 55 units daily. In spite of this and local measures, the gangrene slowly extended. On January 14 consent was finally obtained for operation. With full realization of the odds against any conservative attempt, it was decided to make a trial, at least for the instructiveness.

Therefore, on January 14 a narrow tourniquet was applied above the ankle, and the foot was immersed in ice water to a level a little above this for one and one-half hours. The patient ate part of his lunch while waiting outside the operating room and the remainder after the end of the operation. By removal of the second and third toes and the ends of the corresponding metatarsal bones it was possible to eliminate the gangrenous area, although there was a dangerous encroachment on the fourth toe and its metatarsal. Only slight bleeding needed to be checked after release of the tourniquet. The skin and the soft tissues could not be approximated but were drawn slightly together with silk. The blood pressure was 158 systolic and 80 diastolic before the operation, probably from nervousness, but it soon fell and remained at 130 systolic and 64 diastolic.

The usual light dressing and ice bags were applied, but the patient was unruly and managed to keep his foot warm most of the time. The interior of the wound became a black sloughing mass. Healing was impossible, and consent for amputation was obtained.

On February 1 the leg was refrigerated, and amputation was performed through the lower third of the tibia. Two soft rubber drains were used. The patient's psychic state resulted in irregular postoperative cooling with the ice bags in place only part of the time. A part of the wound healed by first intention; there was a superficial slough laterally which on separation left a clean granulating surface.

The production of any real suffering by cold is a reason for omitting refrigeration or for proceeding with great care, but this and the preceding case illustrate mishaps due entirely to psychic difficulties. It remains unknown whether healing could have been obtained by efficient cooling after the ultraconservative first operation in such a case, but there is no doubt that cold assisted in checking tissue breakdown and infection. The

Fig. 3.—Recent supracondylar amputation done with refrigeration and higher amputation performed two years previously by older method.

final operation illustrates healing under refrigeration in the customarily forbidden region of the lower part of the tibia.

Case 6.—A Greek cook aged 66 years was admitted on Nov. 27, 1940 with arteriosclerotic gangrene and sepsis. He complained of pain in the legs which had progressively increased for six months. He had cramps in the legs in walking and had had a series of ulcers on the legs during the preceding six years; he had had injections for varicose veins three years before admission.

The findings on admission were: temperature, 101 F.; pulse rate, 120; blood pressure, 178 systolic and 96 diastolic; urine and chemical composition of the blood, normal. The right leg showed numerous pigmented scars of old ulcers. The left leg was atrophic and indurated; a dirty ulcer covered two thirds of the medial and posterior surfaces and exposed the achilles tendon.

Septic temperatures persisted despite treatment, and the constitutional condition was serious. On account of good pulsations and oscillometric readings at and

below the knee, it was decided to perform amputation through the calf muscles. This was done on December 19 with the patient under anesthesia induced with a morphine salt and scopolamine hydrobromide and with the site of operation under local anesthesia induced with procaine hydrochloride. The flaps were closed with a drain, which was removed after twenty-four hours. Sloughing followed.

All these events occurred in another surgical service, and on transfer of service the patient was found with the bones of the knee exposed and purulent infection extending above the joint. His temperature ranged from 97.5 to 101 F., with a disproportionately high pulse rate. The hemoglobin content was 76 per cent. The leukocyte count was 10,000, with 76 per cent polymorphonuclears. The patient was considered moribund and unfit for operation.

As the refrigeration method had just been adopted, it was applied in this case by surrounding the stump with bare ice bags to reduce the skin temperature to almost freezing. Immediately the discharge was reduced to about a tenth of the previous quantity, and the local and general conditions showed marked improvement within twenty-four hours. This immediate result with refrigeration was obtained after three days of the administration of sulfathiazole had shown no perceptible effect. A blood transfusion was then given, and on the next day (January 21) a tourniquet was applied at the midthigh and ice packed about the limb for two and one-half hours. Amputation was then performed in the lower third of the thigh, barely above the uppermost pocket of visible pus. The edges were drawn together only partially, leaving plenty of open drainage space. After operation, thin dressings and continuous application of ice bags were employed. The patient was immediately comfortable and gained rapidly in strength and appetite. The exposed muscles remained pink and fairly clean, but with any attempt to withdraw the ice bags an unhealthy color and a foul discharge appeared.

Toward the middle of February, with the local condition and general strength still good, a slight elevation of temperature was explained by the finding of an indurated area high up on the posterior surface of the thigh. In lieu of any other treatment, an ice bag was applied to this area for the first time. Slowly a fluctuant area developed, and an incision was made almost to the ischial tuberosity. Slough and thin pus were evacuated, and after two weeks the clean granulating posterior surface of the thigh was covered with a skin graft.

Case 6 illustrates a type of trouble which is familiar under the customary surgical methods, also the service of the new method in avoiding shock and checking infection. With reference to preservation of tissue vitality, it is noteworthy that no sign of trouble developed in tissues which were made bloodless by the tourniquet at operation or which were later chilled with ice bags; the secondary infection occurred only above this zone.

Case 7.—A Jewish building superintendent aged 49 years was admitted to a hospital with diabetic gangrene and infection. He gave a history of ten years of mild diabetes treated with diet only. Polydipsia and polyuria had long been present. One month before admission gangrene began in the left great toe and became steadily worse. The gradual increase of intoxication and fever was not checked by several courses of treatment with sulfanilamide and sulfathiazole. Finally, he was given insulin and transferred to City Hospital, with the diagnosis of an inoperable condition, on Jan. 31, 1941.

Examination showed a pale flabby obese man who was conscious and able to speak faintly and who complained of coldness and chills. There were coarse tremors of the extremities and cold perspiration. The temperature was 104 F. The pulse rate was 110 and extremely weak. The respiration rate was 28. The blood pressure was 100 systolic and 55 diastolic. The urine was free from sugar and acetone. The blood sugar was 105 mg. The Wassermann test was negative. The red blood cell count was 3,200,000; the leukocyte count was 11,000 with 92 per cent polymorphonuclears. A blood culture yielded no growth. The abdomen was pendulous and soft. All the viscera were normal. Palpable pulses were absent in both popliteal arteries and below. The left foot was swollen to nearly twice the normal size; multiple perforations in the sole discharged pus and slough. Edema diminished gradually up to the knee, and streaks of lymphangitis were visible up to the midcalf. Collections of yellow pus, rather extensive but superficial, also were present on the right ankle and the upper lateral aspects of both thighs.

An intravenous infusion of 1,000 cc. of physiologic solution of sodium chloride with 5 per cent dextrose was given without perceptible change in the condition. A tourniquet was applied just below the knee and the leg refrigerated as usual. The patient lost consciousness briefly whenever raised up or moved. After only one and one-half hours of refrigeration the leg was amputated a little below midcalf; a slight burning pain was experienced when the nerves were cut. In spite of marked thickening of the arteries, the tissues were bright colored and the blood supply apparently adequate, except on the medial aspect. Here a thick column of wet dark necrotic subcutaneous tissue extended to a level above the circular incision. It was trimmed out with scissors to a point about 2 inches (5 cm.) higher, where the dark color changed to a somewhat cooked appearance of the tissues. This pocket and the entire wound were packed with gauze soaked in cod liver oil. The usual ice bags were applied over light dressings.

At the time of beginning the operation the blood pressure had fallen to 65 systolic and 40 diastolic. A continuous record during the operation showed the maximum blood pressure to be 75 systolic and 50 diastolic, the minimum, 60 systolic and 42 diastolic, and the final, 65 systolic and 42 diastolic. After the operation a transfusion of 300 cc. of citrated blood was given, and subsequently another infusion of 1 liter of physiologic solution of sodium chloride with 5 per cent of dextrose, accompanied by 25 units of insulin was given subcutaneously. The patient was irrational at times during the night but drank some fruit juice and in the morning announced that he was feeling much better. His temperature was normal. The dressings were brightly stained with the serosanguinous discharge characteristic of refrigeration. The surface temperature of the stump was 23 C (73.4 F.). The administration of sulfathiazole was then begun with a dose of 4 Gm. followed by 1 Gm. every four hours.

With steady improvement the temperature remained normal except for unimportant elevations at times when pus was retained in the wound. The temperature of the stump was kept near 22 C. (71.6 F.). On February 7 the administration of sulfathiazole was discontinued. The blood pressure was 148 systolic and 88 diastolic.

The stump became clean, and healthy granulations appeared. Several superficial abscesses appeared on the trunk. After a two week period during which the patient had been in a chair, a chill appeared with a subsequent septic type of temperature. The urine was found to be loaded with pus. The patient now began

to go steadily downhill and twenty-four hours before death had a cerebral accident which caused loss of consciousness and right hemiparesis. Death occurred five weeks after amputation with a clean healing leg stump showing no evidence of local infection. There was no autopsy.

CASE 8.—An 83 year old man with senile arteriosclerotic gangrene was admitted on Feb. 3, 1941. Six months previously he had struck his right foot against a door, and it had remained painful thereafter. He was received by transfer from another hospital, where the great toe had been amputated. His temperature was 99.4 F. The pulse rate was 100. The respiration rate was 28. The blood pressure was 160 systolic and 0 diastolic. The blood and the urine were normal. The aortic second sound was accentuated. There were a few coarse rales at the bases of the lungs. General arteriosclerosis was marked; also marked was muscular atrophy, especially in the legs. No pulsations were palpable from either knee downward. There was profuse suppuration at the site of the missing right great toe, involving most of the sole. The dorsum was bright red, the entire foot was swollen to twice normal size, and streaks of lymphangitis extended a considerable distance up the calf. Amputation was performed immediately.

A tourniquet was applied close below the tubercle of the tibia, and the leg was refrigerated in ice for one hour. The amputation was done at about midcalf, within the area of evident lymphangitis. As the leg was thin, it seemed that the preparation would be easy; but although the tourniquet was tightly applied, it failed to overcome the bony protection of the artery. The usual bold circular cut caused a hemorrhage until the arteries were clamped, and because of the poor arrest of circulation the anesthesia was not perfect. The wound was closed with a small drain at each angle. The usual thin dressings and ice bags were applied, and a transfusion was given.

On subsequent days the ice bags were gradually reduced and the dressings made thicker, until on the sixth day all refrigeration was discontinued. Healing was by primary union, although it was slow. The flaps were long, and a posterior molded plaster splint helped to hold them in position.

There were several elevations in temperature to 101 or 102 F., apparently explainable by mild cough and rales in the lungs. In spite of some use of sulfathiazole, the attacks recurred, until on February 15 there was a more severe attack with a rise of the temperature to 104 F. Although the absence of consolidation was noted by roentgen and other examinations of the lungs, it is highly probable that the patient would have died except for a vigorous course of treatment with sulfathiazole, which produced a vivid rash and also an abrupt fall of the temperature to normal. Apart from this complication the patient was not appreciably disturbed by the operation and retained excellent appetite and spirits. The stump healed nicely, and after a period in a wheel chair he was discharged.

Delayed shock or the tax on the strength in connection with healing is the essential danger in a case such as this. Therefore, in addition to the shockless operation, the ability to restrict the amputation to a small part of the leg instead of a thigh appears to be an important advantage. The successful healing in the presence of arteriosclerosis, atrophy and infection gives encouragement concerning future possibilities under right management.

Data on Forty-Five Cases in Which Reduced Temperatures Were Used in Connection with Amputations for Peripheral Vascular Disease

Patient	Age, Yr.	Sex	Race	Disease	Local Condition	General Condition	Site of Amputation	Survival Period *
1	82	M	W	Diabetes and arteriosclerosis	Gangrene of both feet	Poor	Lower part of thighs (2)	21 days
2	64 (?)	F	W	Arteriosclerosis	Gangrene of foot	Fair	Lower part of thigh	14 days
3	72	M	W	Diabetes	Gangrene of foot	Poor	Lower part of leg	4 days
4	51	M	N	Arteriosclerosis	Gangrene of foot and leg	Fair Poor	1. Lower part of leg 2. Higher part of leg 3. Lower part of thigh	
5	68	M	W	Diabetes and arteriosclerosis	Gangrene of foot	Poor	1. Foot 2. Midleg (closed)	
6	66	M	W	Arteriosclerosis	Gangrene of foot	Poor	7. Gastrocnemius muscle (Callander amputation) 2. Lower part of thigh 3. Incision and drainage 4. Skin graft	
7	49	M	W	Diabetes	Gangrene of foot and infection	Very poor	Midleg (open)	6 weeks
8	83	M	W	Arteriosclerosis	Gangrene of toes	Fair	Midleg (closed)	
9	72	F	N	Diabetes and arteriosclerosis	Gangrene of foot	Very poor	Lower part of thigh	6 days
10	67	M	W	Diabetes	Gangrene of foot	Fair	Midleg	
11	67	M	W	Diabetes (insulin resistant)	Gangrene of foot	Very poor	Midleg	5 days
12	50	F	N	Arteriosclerosis	Gangrene of foot and ankle	Fair	Midleg	
13	56	F	W	Embolism	Gangrene (?) of leg	Poor	Lower part of thigh	
14	65	F	N	Diabetes and arteriosclerosis	Gangrene of foot	Poor	Lower part of thigh	
15	79	M	W	Diabetes and arteriosclerosis	Gangrene of foot	Very poor	Lower part of thigh	
16	71	M	W	Arteriosclerosis	Pain	Fair	Midleg	
17	73	M	W	Diabetes and arteriosclerosis	Gangrene of foot	Poor	1. Midleg 2. Lower part of thigh	
18	83	M	W	Arteriosclerosis	Gangrene of foot	Poor	Midleg	
19	58	M	W	Diabetes and arteriosclerosis	Gangrene of foot	Poor	Lower part of thigh	
20	78	M	W	Diabetes and arteriosclerosis	Gangrene with infection	Very poor	1. Midleg 2. Lower part of thigh	
21	69	M	W	Diabetes	Gangrene of foot	Fair	Midleg	
22	74	M	W	Diabetes	Gangrene of foot	Fair	Midleg	

				arteriosclerosis	infection			
21	69	M	W	Diabetes	Gangrene of foot	Fair	Midleg	
22	74	M	W	Diabetes	Gangrene of foot	Fair	Midleg	
23	50	M	W	Chronic osteomyelitis of foot and leg	.....	Good	1. Midleg 2. Lower part of thigh	
24	60	F	N	Diabetes	Gangrene of foot	Fair	Lower part of thigh	
25	64	F	W	Diabetes	Gangrene of foot	Good	Midleg	
26	57	M	W	Arteriosclerosis	Gangrene of foot	Fair	Lower part of thigh	
27	69	M	W	Arteriosclerosis	Gangrene of foot	Fair	Lower part of thigh	
28	76	M	W	Arteriosclerosis	Gangrene of foot	Very poor	Lower part of thigh	
29*	78	M	W	Diabetes and arteriosclerosis	Gangrene of foot	Very poor	1. Lower part of the right thigh 2. Lower part of the left thigh	
30	71	F	N	Diabetes and arteriosclerosis	Gangrene of foot	Poor	Lower part of thigh	
31	65	M	W	Diabetes	Gangrene of foot	Fair	Lower part of thigh	
32	74	F	W	Diabetes and arteriosclerosis	Gangrene of foot	Poor	Lower part of thigh	
33	60	M	W	Arteriosclerosis and frostbite	Gangrene of foot	Fair	Lower part of thigh	
34	83	M	W	Arteriosclerosis	Gangrene of foot with infection	Fair	Midleg	
35	85	M	W	Arteriosclerosis	Gangrene of foot	Poor	1. Midleg 2. Debridement for gas gangrene 3. Guillotine through the lower part of thigh	Died 50 hr. after third operation
36	54	F	W	Diabetes, hyperthyroidism and arteriosclerosis	Gangrene of foot	Poor	Lower part of thigh	
37	65	M	W	Diabetes	Gangrene of foot	Poor	Midleg	4 months
38	62	M	W	Syphilis, arteriosclerosis and old frostbite	Gangrene of foot	Fair	1. Amputation of toes 2. Midleg 3. Lower part of thigh	
39	76	M	W	Arteriosclerosis	Gangrene of foot	Fair	1. Midleg 2. Lower part of thigh	
40	72	M	W	Arteriosclerosis and diabetes	Gangrene of both feet	Poor	1. Lower part of the left thigh 2. Lower part of the right thigh	
41	56	F	N	Arteriosclerosis	Gangrene of foot	Fair	Lower part of thigh	
42	56	F	W	Diabetes	Gangrene of foot	Poor	Lower part of thigh	
43	77	M	W	Arteriosclerosis	Gangrene of foot	Poor	Lower part of thigh	
44	67	M	W	Arteriosclerosis and diabetes	Gangrene of foot	Good	Disarticulation at knee (amputation had been done through midthigh on other side three years previously)	
45	51	F	W	Diabetes	Gangrene of foot and ankle	Fair	Lower part of thigh	

* Patients for whom no survival period is indicated are alive at the time of writing.

CASE 9.—The patient was a 73 year old Negress. She was received in poor condition but underwent an amputation through the lower part of the thigh with the usual absence of perceptible shock. Refusal of food during one week before operation was considered probably due to intoxication. Continued refusal after operation was also presumed at first to be temporary and largely psychic. As the stump remained in perfect condition and the entire picture was different from infection, the nature of the cachexia which proved fatal remained undetermined.

ANALYSIS OF DETAILS IN THE TABLE

A survey of the total series of 45 cases is given in the table. Thirteen of the patients were women. Seven of the patients were Negroes.

The major operations performed on the 45 patients numbered 57. All but 9 patients survive at the time of writing. Omitting 2 deaths at two and nine months, respectively, i. e. after the stumps were thoroughly healed, the number of deaths for calculation is 7. In 4 of the cases in which death occurred the survival periods were, respectively, two, four, five and six days, and in the 3 others two, three and six weeks. Only 1 death is admitted as due directly to the operation or to an unsatisfactory condition of the wound. This death (case 3) occurred in the earliest stage of inexperience and could presumably have been avoided with the advantage of later knowledge. The other deaths were attributable to medical complications or to septicemia or other fatal conditions antedating the operation. Inclusion of the entire 7 deaths occurring within six weeks or less after amputation gives a gross mortality rate of 15.5 per cent among the 45 patients or 12.3 per cent for the 57 major amputations. These figures based on an entirely unselected series represent a great statistical improvement over results previously obtained with patients in extremely poor average condition admitted to this public hospital.

Various details may be further analyzed as follows: With the aid of refrigeration it proved feasible to avoid amputation through the upper part of the thigh throughout the series. Among the 57 amputations in connection with which refrigeration was used, 21 were through the leg and 36 through the lower part of the thigh. With the amputations through the lower part of the thigh there were 4 deaths (mortality rate 11 per cent) and no failures of healing. With the amputations through the leg there were 3 deaths besides 5 failures of healing. Inasmuch as the deaths in general are not considered due to the operations, these figures are not a criterion of the relative safety of the two sites. Obviously, failure of healing is more likely at the lower site. However, successful healing was obtained in the leg in 13 cases, although in most or all of these the patients would have been candidates for higher operations without the refrigeration method. Also 1 death among the 8 reamputations contrasts with the prevalent idea of a high or prohibitive mortality rate and is evidence of the comparative safety of at

least trying the lower site when it is desired either to avoid constitutional strain or to preserve the knee joint.

COMMENT

Successful results require attention to technical details. Some of these are still undecided, but several can be mentioned provisionally as follows:

The tourniquet is a pure gum rubber tube, usually about 1 cm. in diameter. It is applied in two or, if necessary, three turns, one superimposed on the other to make the narrowest possible zone of compression. Unnecessary pain is caused by folds of the skin and can be largely prevented by care to avoid such folds and by preliminary chilling of the skin. Preliminary sedation is useful for nervous or apprehensive patients but is not needed for others. The eyes are covered, or a screen is interposed so that the patient does not see the operative field; stopping his ears with cotton prevents him from hearing the saw.

The tightness of constriction necessary to stop circulation differs with the patient, the location on the limb and other variables. Difficulties seem to be less in the thigh, in spite of its thickness, than in the upper part of the calf, where the main artery is protected between bones. Success may be had with a tourniquet above the knee or below the tubercle of the tibia but probably never between these levels. A little dark blood may accumulate as the result of inflow through the vessels of the marrow, especially of the tibia. It is prudent to inspect the limb one or more times twenty or thirty minutes after beginning refrigeration. Blanching of the foot is the rule, especially if the leg was elevated before applying the tourniquet. If any sizable arteries remain open the foot will be darkly cyanosed, and some error in the tourniquet should then be corrected. Any influx of blood makes for incompleteness or delay of anesthesia.

The optimum extent of preparatory refrigeration is undecided and is partly a matter of personal choice. Our experience with thin, weak patients with arteriosclerosis has definitely determined the time as follows: for the thigh, two and one-half hours; for disarticulation at the knee or through the middle of the leg, two hours; for the lower half of the leg or the foot, one and one-half hours; for the metatarsus or the toes, one hour. If the tourniquet is properly applied and securely fastened and the chilling is continuous to all parts at the correct temperature, there is complete local anesthesia so that the patient is not aware when the nerve is cut or the bone sawed.[2a] Likewise there is no certainty whether the tourniquet should be prudently placed close to the

2a. Crossman, L. W.; Ruggiero, W. F.; Hurley, V., and Allen, F. M.: Ice Water Anesthesia for Leg Amputations, J. Internat. Cong. Anesthetists, to be published.

site of amputation, so as to leave the narrowest possible zone of chilled and bloodless tissue, or whether it may be fearlessly placed high, for example above the knee for amputation through the calf. It can only be said that no harm has been demonstrated thus far from either duration or extent of refrigeration. Marks resulting from the tourniquet have been visible for a day or two but have not proved significant. Contracture or paralysis has not resulted. More important, there has been no sign of thrombosis or other damage to blood vessels, and no special tendency to necrosis or infection indicating lowered resistance of tissues. The experience is not extensive enough to prove that such injuries will never occur, and for this reason positive rules are not yet formulated. Inasmuch as temperatures slightly above freezing have permitted animals' legs to survive more than two days without circulation,[3] and rats' tails, four days or more,[4] there seems theoretically to be little danger even to diseased limbs from the comparatively short periods of refrigeration employed clinically.

Obviously, everything warm should be kept away from the tissues during operations. Iced solution of sodium chloride has been used in connection with sawing and for other purposes. The object in view is not merely anesthesia of nerves but also anesthesia of protoplasm in order to prevent shock and injury to the vitality of the tissue. Possible adjuvant devices, such as keeping the limb on a bed of ice bags or a cold atmosphere for the operating room, have not appeared necessary for short operations but may be advisable for plastic and other long procedures.

As usual, undermining and dissection of tissues are avoided as far as possible. For amputations either through the calf or through the lower part of the thigh we have used modifications of the procedures devised by Dr. A. G. Fuller and introduced to City Hospital by Dr. F. W. Bancroft.[5] Allowing rather liberal pads of soft tissue has seemed

3. Allen, F. M.: Surgical Considerations of Temperature in Ligated Limbs, Am. J. Surg. **45**:459, 1939; Resistance of Peripheral Tissues to Asphyxia at Various Temperatures, Surg., Gynec. & Obst. **67**:746, 1938; Ligation and Refrigeration of Intestine, Surgery **3**:893, 1938; Physical and Toxic Factors in Shock, Arch. Surg. **38**:155 (Jan.) 1939; footnote 1a.

4. Brooks, B., and Duncan, G. W.: The Effects of Temperature on the Survival of Anemic Tissue, Ann. Surg. **112**:130, 1940.

5. Low Thigh Amputation: With the Ruggiero modification a circular incision is made at the level of the lower border of the patella. All soft tissues are divided at this level, the knife traverses the knee joint, and the leg is removed. By dropping the end of the table the operator now faces the stump. The patella is turned up and dissected from its capsule. The soft tissues are freed anteriorly from the femur and on both sides. Posteriorly the shaft is bared, leaving undisturbed the attachments of the gastrocnemius, popliteus and plantaris muscles. The shaft of the femur is now divided about 2 inches (5 cm.) above the condyles. The main vessels are ligated, and the tourniquet is released. Bleeding points are

advisable, especially in the lower leg. Tightness is certainly to be avoided. Possibly because of the shrinking action of cold, primary union has apparently been favored in the danger zones by flaps which would ordinarily be considered as somewhat redundant.

The usual dressing after amputations has consisted of one layer of petrolatum gauze across the wound, then a few layers of dry gauze, surrounded by bare ice bags, for example one bag beneath and two sloping tentlike bags at the sides to avoid pressure on the limb. Often the desired skin temperature has been set arbitrarily at 15 C. (59 F.) for the first day after operation and has been raised gradually during the following days or even weeks. Until controllable apparatus is available, one method for gradually raising the temperature is to make the dressings a little thicker day by day. Both the degree and the duration of cooling are thus far entirely empiric and guided by the appearance of the wound. Sutures must be left in for an unusually long time. Healing is slowed in proportion as the temperature is kept reduced; therefore the temperature is raised as rapidly as conditions permit. In the experience to date, failures appear to have been chiefly due to mistaken judgment or inadequate regulation of postoperative temperature.

A number of broad questions of principle arise, of which only two will be mentioned briefly.

The optimum level of amputation is undecided, and there is uncertainty how far it may be changed by refrigeration. The work was begun [1] with a theoretic preference for low levels because of delayed shock and the strain of healing large wounds in weak patients and because of the better functional results which should be possible with proper prosthetic aids when the knee joint is preserved. Furthermore, deep postoperative chilling is more efficient in the leg than in the thigh. Therefore, the work has often contravened accepted rules, at least for experimental purposes. Operations have been performed at forbidden levels; areas of known infection have been cut across and then closed tightly or with only small drains. Granting that infectious organisms

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ligated, and the deep fascia is closed transversely by interrupted sutures. The skin is closed in a similar manner. A moderate-sized dressing is applied, and the stump is placed on a posterior molded plaster splint.

Leg Amputation: The preferred site is the midleg, just below the bellies of the gastrocnemius muscle. A circular incision of the soft tissues is combined with a vertical incision over the lateral border of the fibula so that this bone may be removed at a level 3 inches (7.6 cm.) above the circular incision without extensive dissection. For convenience the fibula is first divided at the level of the circular incision and again 3 inches (7.6 cm.) higher. The tibia is now approached along the interosseous membrane and divided 2 inches (5 cm.) above the circular incision. The sharp anterior border is thoroughly beveled off. Closure is made by interruptured sutures in the deep fascia and in the skin. Silk technic is routine for sutures and ligatures.

are invisibly present in such legs up to the groin, a reason may be found for occasional mild or brief febrile attacks, and the question may be raised whether these are more debilitating or dangerous than a higher amputation. Excepting case 3, which represents mistakes of management in the pioneer period, the infectious dangers have largely been overcome with refrigeration. Even the sloughing of flaps after unduly low amputations has been confined to a narrow zone, entailing no important systemic disturbances and permitting of easy reamputation.

Misgivings have existed whether unduly severe or prolonged chilling may reduce local vitality, weaken physiologic barriers to diffusion so as to facilitate the penetration of bacteria or their products into the general circulation or create dangers of thrombosis or embolism. The extensive use of cold in another manner by Fay and a recent striking observation by McElvenny[6] tend to oppose these suppositions. In the present series every death has had a rational explanation in an existing complication. Even if immediate operative shock is entirely prevented, some deaths may still be induced in enfeebled patients by delayed shock and the general strain of wound healing. The remarkably good preservation of general strength, the practical absence of postoperative pain or need for sedatives, the retention of appetite and spirits, the limitation of necrosis or infection even under unfavorable conditions and the total absence of thrombosis or embolism all testify to the lack of injury from either the reduced temperature or the tourniquet and establish the life-saving value of the new method in the surgical treatment of peripheral vascular disease.

SUMMARY

The experience in a series of 45 cases has convinced us of the value of the refrigeration method for amputations. Further improvements may be hoped for with the gaining of more knowledge of optimum postoperative temperatures and the introduction of apparatus for maintaining such temperatures. It is believed that the principle will find wider uses, and at the present time its adoption for emergency and military operations is particularly to be emphasized.

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6. McElvenny, R. T.: The Effect of Cooling Traumatized and Potentially Infected Limbs, Surg., Gynec. & Obst. **73**:263, 1941.

LYMPHOSARCOMA OF THE RECTUM

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Lymphosarcoma of the rectum is rarely recognized as such before histologic study of the tissue has been made. In 1929, Rankin and Chumley [1] reported a series of 18 cases of lymphosarcoma of the colon and the rectum. The location of the tumors was as follows: Thirteen were in the cecum; one was in the descending colon; one was in the sigmoid; and three were in the rectum. In 1933, Smith [2] found 17 recorded instances of lymphosarcoma of the rectum and the sigmoid and added the cases of 6 patients who had been treated at the Mayo Clinic since 1926. Raiford [3] reviewed a series of 45 cases of lymphoid tumor of the gastrointestinal tract from the Johns Hopkins Hospital. The distribution was as follows: In 13 the tumor was in the stomach; in 1, in the duodenum; in 19, in the ileum; in 11, in the colon, and in 1, in the rectum. Lynch and Hamilton [4] recently reported 3 more cases. Pattison [5] in reporting a series of 6 cases of malignant lymphoma of the gastrointestinal tract described 1 tumor involving the rectum.

According to Rankin and Chumley, the clinical diagnosis of lymphosarcoma of the rectum is rarely suspected before operation since there are no characteristic features which might be used to distinguish it from the tumors more commonly found in this region. These tumors predominantly affect men. Sutton [6] stated that the growths are apt to be

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1. Rankin, F. W., and Chumley, C. L.: Lymphosarcoma of the Colon and Rectum, Minnesota Med. **12**:247-253 (May) 1929.

2. Smith, N. D.: Lymphosarcoma of the Rectum and Sigmoid, Proc. Staff Meet., Mayo Clin. **8**:437-438 (July 19) 1933.

3. Raiford, T. S.: Lymphoblastomas of the Gastrointestinal Tract, Arch. Surg. **26**:813-835 (May) 1933.

4. Lynch, J. M., and Hamilton, G. J.: Lymphosarcoma of the Rectum, Tr. Am. Proctol. Soc. **40**:221-226, 1939.

5. Pattison, A. C.: Malignant Lymphoma of the Gastrointestinal Tract, Arch. Surg. **29**:907-922 (Dec.) 1934.

6. Sutton, C. J.: Primary Lymphosarcoma of the Rectum, Canad. M. A. J. **26**:71-73 (Jan.) 1932.

located in the lower portion of the rectum. The inguinal nodes may be involved.

Grossly, tumors diagnosed as lymphosarcoma are divided into the polypoid and the diffuse infiltrative type. The polypoid formations are firmer in consistency than the softer adenomatous polyps. The surfaces made by sectioning the gross specimen often have a homogeneous pale gray surface resembling brain tissue which has been fixed in solution of formaldehyde. The process extends along the submucosa and at first forms a localized submucosal thickening which by pressure may cause necrosis or which may invade the mucosa. Later, ulceration and bleeding may follow. In some instances the mucosa may move freely over the tumor mass. The tunica muscularis is invaded and replaced by lymphoid tissue. In many of the reported cases the infiltration does not extend beyond the serosa. Lynch and Hamilton noted that the lines of cleavage are more easily demarcated than those one usually encounters with carcinoma. In a case described by Martin,[7] the rectal valves had a thickened appearance, and there were several adjacent ulcerated areas, but the process did not grossly give the impression of being malignant.

REPORT OF A CASE

A man 27 years of age was admitted to the Grant Hospital complaining of a mass which protruded at times from the anus. He had noticed also some bleeding from the anal region, which he attributed to hemorrhoids. There was no history of injection treatments for hemorrhoids. A roentgen chest plate showed nothing abnormal. Roentgen studies of the colon revealed no abnormalities. A proctoscopic examination was made, and a polypoid mass was noted in the right posterior quadrant of the anus about 0.5 cm. above the pectinate line. One pea-sized polyp was fulgurated near the rectosigmoid junction. No biopsy was made. The remaining mucosa was normal. The polypoid tumor mass was excised by removing the skin distal to it and removing about 1 cm. of mucosa around the tumor. The mucosa was dissected from the external and internal sphincters and the hemorrhoids removed. The lobulated sessile tumor mass measured 2.3 by 1.5 by 1.0 cm. The cut surface was homogeneous pale gray and firm.

Microscopic Description.—There were large areas of lymphoid cells surrounded by varying amounts of connective tissue. The infiltrations involved the submucosa, the tunica muscularis and the subserosa. In some places the mucosa was invaded by lymphoid cells, and in others the main tumor mass caused atrophy of the mucosa by pressure. The type cell was slightly larger than a lymphocyte. There were a few larger cells with a moderate amount of cytoplasm. In the centers of some of the larger lymphoid areas, the cells were less closely packed than at the periphery, and there were a few larger lymphoid cells measuring twice the diameter of the predominant cell. These large lymphoid islands resem-

7. Martin, W. C.: Lymphoblastoma of the Gastrointestinal Tract, Am. J. Roentgenol. **36**:881-891 (Dec.) 1936.

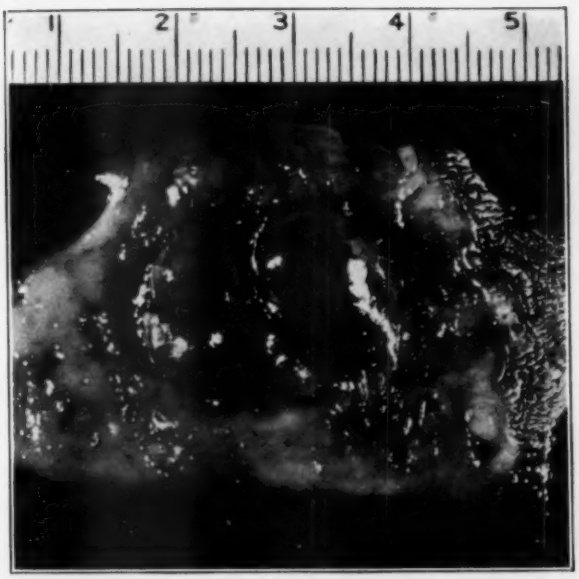

Fig. 1.—Polypoid tumor mass, measuring 2.3 by 1.5 by 1.0 cm., which was located just above the anal margin.

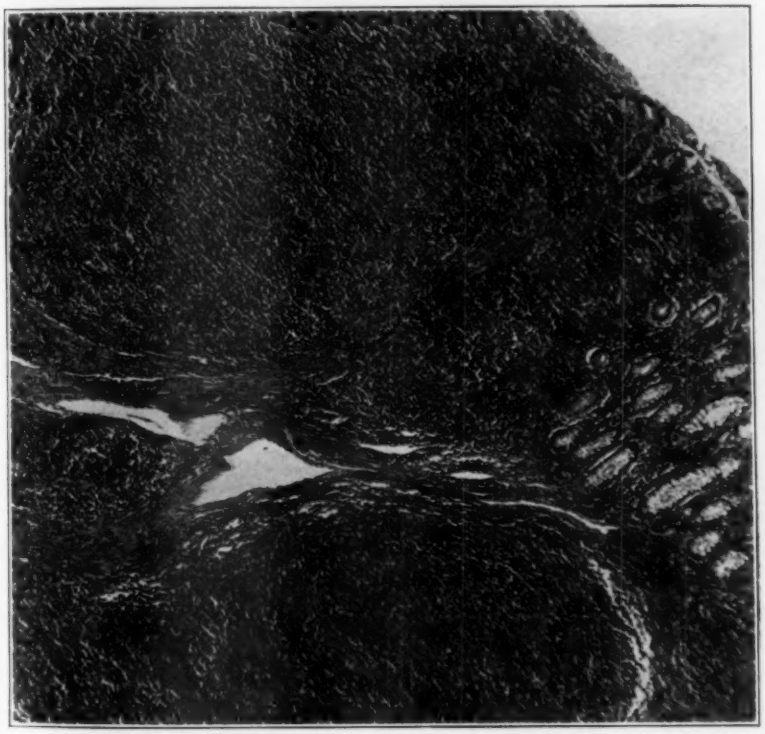

Fig. 2.—Photomicrograph (× 40) showing the large islands of lymphoid tissue surrounded by various amounts of connective tissue. These structures extended from the mucosa to the serosa.

bled somewhat a giant follicle, but there was no definite cortical layer of delimiting cells, and the large lymphoid areas fused in many places. There were a few small foci of inflammatory cells, including plasma cells, eosinophils and polymorphonuclear leukocytes. These were located in the compressed submucosa, which was not invaded by lymphoid cells. There were also some pigment-laden macrophages in the submucosa. The Perdrau silver stain for reticulum fibers showed large areas with only a few reticulum fibers. A few areas showed numerous reticulum fibers.

Fig. 3.—Photomicrograph showing under higher magnification (× 112) the diffuse lymphoid infiltrations which extended into the mucosa, causing ulceration and bleeding.

COMMENT

According to Ewing,[8] there are two general types of lymphosarcoma arising in lymphoid tissue. They are the large round cell lymphosarcoma or reticulum cell sarcoma and the small round cell sarcoma or malignant lymphocytoma. The tumor described in this paper falls under the latter

8. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 424.

classification. Symmers [9] objected to the term "reticulum cell lymphosarcoma" and suggested that the more appropriate term is "large round cell sarcoma." Krumbhaar [10] stated that the lymphocytic type is more radiosensitive than the reticulum cell type, and according to Raiford the small cell type is the less malignant. Many of the lymphoid tumors of the lymph nodes and of the gastrointestinal tract do not easily fall under a definite classification, and it has been customary for many investigators to group them under the general head of malignant lymphoma or lymphoblastoma. These include Hodgkin's disease, lymphosarcoma of the lymphocytic type, reticulum cell sarcoma, multiple giant follicular lymphadenoma (follicular lymphoblastoma) and others. Mayer and Thomas,[11] quoting Baehr and Rosenthal,[12] stated that lymphoma of the giant follicular type has not been found in the gastrointestinal tract.

Before a diagnosis of relatively early lymphosarcoma of the rectum can be definitely established, chronic inflammatory process and benign lymphoid tumor must be ruled out. Particularly in lymphoid tissue, the transition between simple inflammatory hyperplasia, such as may be seen in tuberculosis, and benign neoplasm of lymphoid character may be difficult to distinguish. Likewise, the transformation from benign to malignant tumor can present similar obstacles in establishing a definite diagnosis. In the gastrointestinal tract especially, according to Ewing,[13] lymphoid tumor may closely resemble infectious granuloma, owing to superimposed chronic inflammatory infiltrations. The tumor reported had a predominantly lymphoid structure with only slight inflammatory foci.

Although the patient gave no history of having had injections for hemorrhoids, the possibility of a rectal tumor of chemical origin was considered, particularly because of the location of the mass just above the dentate margin. Jackman [14] recently described the histologic features of tumors caused by injections of oil, viz., vacuolation and foreign body

9. Symmers, D.: Giant Follicular Lymphadenopathy With or Without Splenomegaly, Arch. Path. **26**:603-647 (Sept.) 1938.

10. Krumbhaar, E. B.: The Lymphomatoid Diseases (the So-Called Lymphoblastomas), J. A. M. A. **106**:286-291 (Jan. 25) 1936.

11. Mayer, S., Jr., and Thomas, H. M., Jr.: Follicular Lymphoblastoma, Bull. Johns Hopkins Hosp. **64**:315-338 (May) 1939.

12. Baehr, G., and Rosenthal, N.: Malignant Lymph Follicle Hyperplasia of Spleen and Lymph Nodes, Am. J. Path. **3**:559, 1927.

13. Ewing, J.: General Pathology of Lymphosarcoma, Bull. New York Acad. Med. **15**:92-103 (Feb.) 1939.

14. Jackman, R. J.: The Differential Diagnosis, Pathologic Aspects and Treatment of Rectal Tumors of Chemical Origin: Report of Cases, Proc. Staff Meet., Mayo Clin. **15**:188-192 (March 20) 1940.

giant cells; neither of these was present in the lymphoid tumor described in this paper. Moreover, the circumscribed character of the polypoid mass, the age of the patient, the location of the mass without signs of adjacent inflammatory changes and the absence of symptoms of tuberculosis, syphilis, fissures, fistulas or trauma together with the insidious onset and the histologic characteristics of neoplastic growth give a composite picture which is incompatible with simple inflammatory hyperplasia.

Since the tumor was fairly well circumscribed and there was no evidence of metastases or invasion beyond the serosa, the possibility of benign lymphoma was considered. In the literature one sees records of cases of borderline lymphoid tumors in which there was difficulty in deciding from histologic studies whether the given tumor was benign, malignant or simply inflammatory. Hayes, Burr and Pruit [15] recently emphasized the limitations which must necessarily be placed on the histologic interpretation of certain lymphoid tumors of the colon and the rectum. They found 20 cases classified in the literature as cases of benign lymphoma. Dukes [16] described 3 instances of benign lymphoid tumor of the rectum and stated that the structure of the tumors consisted of groups of lymph follicles lying in the submucosa and covered by mucous membrane. Two of the patients showed no evidence of recurrence after five years.

In the case that we have described there was definite histologic evidence that we were dealing with a malignant tumor. Of particular importance was the fact that no definite lymph follicle formations, such as may be seen in cases of simple lymphoma, could be found. The large islands of lymphoid cells did not resemble the giant follicles seen in certain forms of lymphoma involving the lymph nodes and the spleen. No analogy can be drawn between the structure of the tumor under discussion and the rare condition described by Ewing [13] as systemic pseudoleukemia; the latter is characterized by many small lymphomas in the mucosa of the gastrointestinal tract, and histologic study shows many well formed lymph follicles. The lack of follicular structure and the fusion of the lymphoid islands indicated a diffuse process. Besides, not only the submucosa was involved but the entire wall from the ulcerated mucosa to the serosa.

Since the histologic structure of the tumor indicated that it was of the less malignant type, the early wide excision of the primary growth may serve to cure the patient. At the time of writing, seven months after the operation, there has been no recurrence, but a guarded

15. Hayes, H. T.; Burr, H. B., and Pruit, L. T.: Lymphoid Tumors of the Colon and Rectum, Surgery **7**:540-545 (April) 1940.

16. Dukes, C.: Lymphoma of the Rectum, with Report of Three Cases, Proc. Roy. Soc. Med. **27**:926-927, 1934.

prognosis must be made in view of the possible lymphoid involvement of other segments of the gastrointestinal tract which may occur years later.

SUMMARY

Lymphoid tumor of the rectum and colon presents an interesting problem in surgery and tumor pathology. The difficulties in the histologic interpretation of lymphoid tumor of the gastrointestinal tract are emphasized. A biopsy of polyps of the rectum and colon and especially of growths near the anorectal region is indicated. The treatment consists of local wide resection of the tumor mass followed by irradiation of the region.

CYSTIC TUMOR OF THE TONGUE

REPORT OF AN UNUSUAL CASE

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The literature contains but few reports of cysts and cystic tumors of the tongue, regardless of type. One would expect these lesions to be encountered more frequently when the numerous glands and the complex embryologic development of this organ are considered.

Cyst formation may result from incomplete obliteration of the lingual portion of the thyroglossal duct. This structure is present in embryos 4 weeks of age (2.5 mm. stage) and normally atrophies during the sixth week of fetal life.[1] Cystic tumors of the tongue are usually situated in the midline beneath the foramen caecum. They are lined by stratified squamous epithelium or by ciliated epithelium.[2]

Mucous or retention cysts result when mucous glands at the base of the tongue become obstructed, with subsequent accumulation of secretion. They have been described most often in infants and may become large enough to produce stridor and asphyxia. They are located between the epiglottis and the foramen caecum and may be either in the midline or laterally placed.[3] In Scheier's [4] case the pharyngeal wall was involved. Retention cysts of Blandin and Nuhn's glands have been reported but are extremely rare.[5]

Wenglowski [6] examined a large number of embryos and cadavers and found numerous small cysts at the base of the tongue. He expressed the belief that these were vestiges of the primitive lingual duct. In the fourth month of embryonic life this duct is broad and branched; small

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1. Arey, L. B.: Developmental Anatomy, Philadelphia, W. B. Saunders Company, 1938.

2. Clute, H. M., and Cattell, R. B.: Ann. Surg. **92**:57-66, 1930.

3. Post, H.: Ztschr. f. Kinderh. **46**:566-568, 1928. Thomas, E.: ibid. **47**: 168, 1929. Vollmer, H.: Klin. Wchnschr. **1**:1212, 1922. Forsyth, E. A.: Laryngoscope **21**:1145-1150, 1911.

4. Scheier, M.: Berl. klin. Wchnschr. **51**:330, 1914.

5. (*a*) Butlin, H. T., and Spencer, W. G.: Diseases of the Tongue, London, Cassel & Company, 1900. (*b*) Fitzwilliams, D. C. L.: The Tongue and Its Diseases, New York, Oxford University Press, 1927. (*c*) Curtis, B. F.: Ann. Surg. **27**:662, 1898.

6. (*a*) Wenglowski, R.: Arch. f. klin. Chir. **98**:150, 1912. (*b*) Colp, R.: Surg., Gynec. & Obst. **40**:183-195, 1925.

portions may become disconnected and form isolated cysts. These cysts have been incorrectly considered dermoids by some authors. Microscopic examination reveals a lining of stratified squamous or ciliated epithelium. The absence of skin appendages differentiates them from true dermoids.

In 1906 Nicoll and Teacher [7] reported a cystic teratoma of the tongue containing derivatives of all three germ layers. Numerous reports of dermoid cysts [8] of the congenital inclusion type involving the floor of the mouth have been published, but no similar cysts occurring in the numerous fusion lines of the tongue have been reported.

Lymphangioma and hemiangioma are occasionally encountered and may involve any portion of the tongue.[9]

In this publication we wish to present the clinical and pathologic features of an unusual tumor of the tongue and to consider also its embryologic aspects.

REPORT OF A CASE

C. W., a Negro boy 2 months old, was admitted to the Vanderbilt University Hospital on Sept. 7, 1939. Shortly after birth he was observed to have an abnormally large tongue. This enlargement progressively increased, and the substitution of feeding by a bottle with a nipple having a large orifice became necessary. The rate of growth was most rapid during the week prior to admission. At the time of admission examination of the child revealed a large tumor in the body of the tongue (fig. 1), displacing the organ upward into the roof of the mouth. The tumor was round and had a faintly bluish hue, visible through the mucous membrane on the dorsal and ventral surfaces of the tongue. In situ it measured about 2.5 cm. in diameter. The tumor was tense, fluctuant and well circumscribed and was easily transilluminated. Preoperative examination revealed a normal sulcus terminalis and a shallow foramen caecum. The papillae and the lingual tonsils also appeared normal.

Operation was performed on September 9 with the patient under ether anesthesia. The tongue was retracted upward by a suture taken through its tip. Incision was made through the mucous membrane covering the ventral surface, and the tumor was dissected free from the surrounding lingual muscle. The muscle was closed with fine interrupted catgut sutures and the mucous membrane with interrupted silk sutures. The wound healed rapidly, and the tongue has since assumed a normal contour.

Gross Appearance of the Tumor.—The tumor measured 2.9 cm. in diameter. The outer surface was smooth. Its consistency was firm but definitely cystic. On incision the cyst was found to be filled with viscid cloudy fluid. The wall measured 2 to 3 mm. in thickness. The inner surface also was smooth in appearance, but on magnification (× 30) small round projections were visible in some areas, while in others there was no elevation or depression.

Microscopic Apearance.—The histologic structure of the cyst was complex (fig. 2). An epithelial lining was present throughout. Stratified squamous

7. Nicoll, J. H., and Teacher, J. H.: Glasgow M. J. **66**:216-222, 1906.

8. New, G. B., and Erich, J. B.: Surg., Gynec. & Obst. **65**:48-55, 1937. Fitzwilliams.[5b] Curtis.[5c] Wenglowski.[6a] Colp.[6b] Nicoll and Teacher.[7]

9. Funk, E. H.: Cavernous Angioma of Tongue, J. A. M. A. **79**:1113-1115 (Sept. 30) 1922. Arrowsmith, H.: Laryngoscope **25**:94, 1915. Tardieu, A., and Dechaume, M.: Rev. de chir., Paris **70**:142-148, 1932. Baumgartner, H.: Schweiz. med. Wchnschr. **55**:1030-1033, 1925. Curtis.[5c] Wenglowski.[6a]

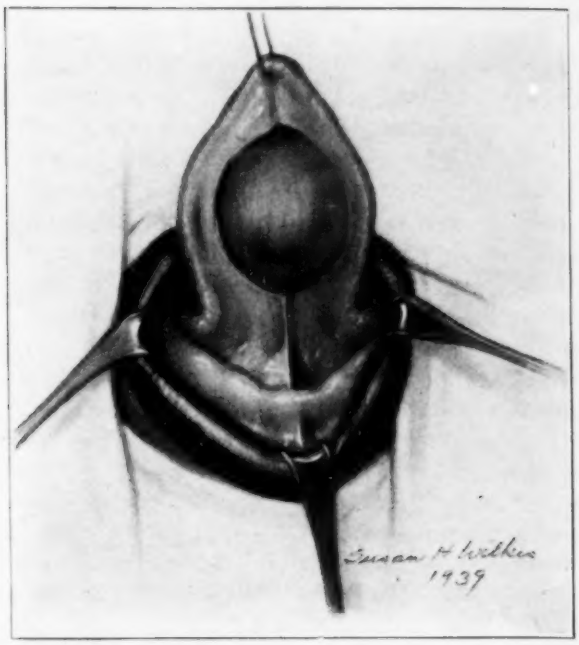

Fig. 1.—Ventral surface of the tongue after the dissection of the mucous membrane from the surface of the tumor.

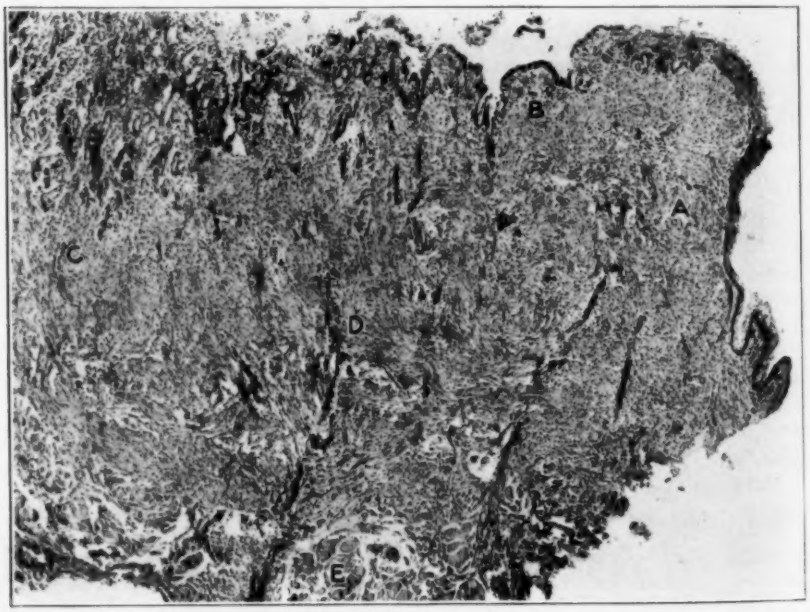

Fig. 2.—Photomicrograph showing the complex histologic pattern of the wall of the tumor: *A*, stratified squamous epithelium; *B*, simple columnar epithelium; *C*, portion containing glands similar to those found in the fundus of the stomach; *D*, smooth muscle; *E*, striated muscle of the tongue.

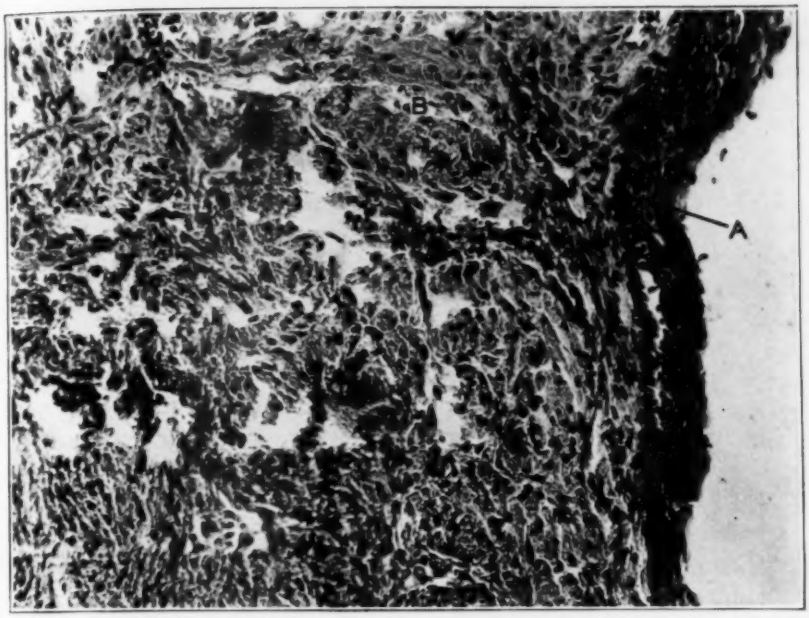

Fig. 3.—Photomicrograph showing the lining of stratified squamous epithelium and the smooth muscle in the wall of the tumor.

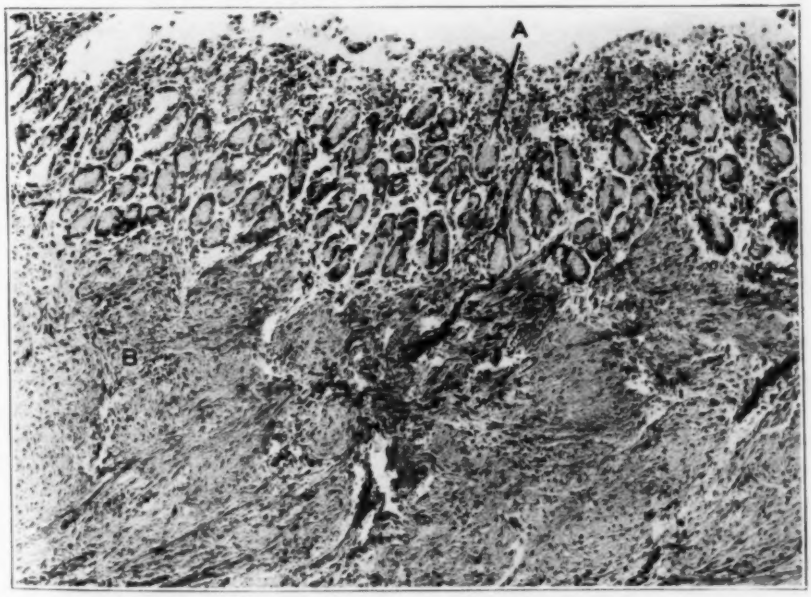

Fig. 4.—Photomicrograph showing higher magnification of a portion of the cyst wall containing (*A*) glands and (*B*) muscular layers similar to those of the fundus of the stomach.

epithelium was seen in some areas, which had the appearance of that normally lining the mouth (figs. 2 and 3). No cornification or skin appendages were present. Other areas were lined by simple columnar epithelium of varying height (fig. 3). Still other areas were lined with mucous membrane similar to that seen in the fundus of the stomach, viz., simple columnar epithelium, with glands showing chief cells, mucous neck cells and parietal cells (fig. 4). The muscularis mucosae and the oblique, circular and longitudinal layers of smooth muscle were demonstrable in this portion. Smooth muscle was present in the entire wall, but the arrangement was much less definite in portions not containing glands and lined by stratified squamous epithelium and simple columnar epithelium. The outermost smooth muscle fibers of the wall interlaced with the striated muscle of the tongue.

COMMENT

Since the tumor described obviously originated early in embryonic life, a brief review of the embryology of the tongue and other related tissues found in the tumor may be helpful in understanding its origin and structure.

The tongue has been described [1] as being primarily of pharyngeal derivation, its forward growth into the mouth being secondary. It consists of two distinct portions, the body or apical portion and the root or posterior portion. These represent different primordia in the embryo and are separated in the adult tongue by the sulcus terminalis. The body or apical portion originates in front of the second branchial arches; the root develops primarily from the second branchial arches but receives contributions also from the third and the fourth. Examination of the pharyngeal floor in the fifth week (5 mm. stage) of embryonic life reveals an unpaired swelling between the first pair of pouches, the tuberculum impar. It was believed by His that the growth of this tubercle formed the body of the tongue. In 1869 Dursy, and later Hammar and other authors, described the organ as having a paired origin.[10] It is now generally accepted that the tuberculum impar lags in development and takes little or no part in the subsequent development of the tongue. The paired lateral lingual swellings formed by the first branchial arches also are visible at the fifth week. Simultaneous with the appearance of these three primordia, the root of the tongue is represented by a medical ventral elevation of the copula which develops by the fusion of the two second branchial arches. The lateral lingual swellings grow rapidly, joining at the median septum and forming the body of the tongue. The copula with the adjacent portions of the second arches increases in size to form the root of the tongue. These fusions are well advanced during the sixth week and are completed soon afterward. The tongue is later encroached on by the third and fourth arches, and there is a general forward dislocation of the mucous membrane. During the

10. Keibel, F., and Mall, F. P.: Human Embryology, Philadelphia, J. B. Lippincott Company, 1912.

seventh week the organ becomes elevated and assumes prominence through the internal development of striated muscle. This muscle belongs ancestrally to the region caudad to the branchial arches, but there seems to be no definite proof that the muscles of the tongue do not arise from the mesoderm of the floor of the mouth.

During the early development of the tongue other related tissues represented in this tumor have begun their development. In the third week of embryonic life the embryonic disk begins to fold into a cylindric mass and carries the endoderm with it into the head region, forming a blind tube, the foregut. This blind tube comes in contact with the ectoderm by the formation of the pharyngeal membrane which separates the foregut from the stomadeum. This membrane ruptures at the beginning of the fifth week of embryonic life, simultaneously with the appearance of the primordia of the tongue. The presence of a fetal cell rest in the floor of the pharynx at the time of appearance of the anlage of the tongue would make possible its inclusion and forward displacement by subsequent growth of the lateral lingual swellings. Forward displacement might also be produced by the anterior migration of the muscle of the tongue, assuming that the muscle arises from the region caudal to the pharynx.

SUMMARY

The clinical and pathologic features of an unusual tumor of the tongue are presented. The embryology of the tongue and of related tissues represented in the tumor is reviewed. The structure of this tumor suggested a cell rest representing more than one germ layer, originating probably between the third and fifth weeks of embryonic life. Its conclusion and forward displacement appear to be definitely related to the development of the tongue.

CORRECTION

In the article by Drs. J. K. Donaldson and E. B. Sive and Mr. Norman Lewis entitled "Intestinal Obstruction," in the November issue (ARCH. SURG. **43**:811, 1941), the first word in the third sentence from the bottom of page 827 should read "Nine" instead of "No."

In the eighth line from the bottom of page 830, "July 1931" should read "July 1939."

COMBINED SURGICAL AND PHYSIOLOGIC TREATMENT OF CRYPTORCHIDISM

DESCRIPTION OF AN OPERATIVE PROCEDURE

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Maldescent of the testis is fairly common; the incidence ranges from 0.2 to 1.02 per cent of the adult male population.[1] Many theories have been evolved and propounded in an effort to explain the causation of this abnormality. These have been summarized and analyzed by several authors.[2]

Many operative procedures for the correction of cryptorchidism have been described. All consist in: (1) lengthening those structures attached to the testis, such as the vas deferens and the blood vessels, so that the testis can be placed in the scrotum and (2) retaining the testis in the scrotum after it has been brought down. Surgeons agree that the cord must be lengthened in order that the testis may be placed in the scrotum. However, there are several differences in the methods of retaining the testicle in the scrotum once it has been placed there.

The more commonly used methods of retaining the testis within the scrotum are: (1) narrowing the neck of the scrotum by sutures to prevent retraction of the testis; (2) suturing the testis to the scrotum; (3) drawing the testis by suture, wire or elastic, to some fixed point outside the scrotum; (4) transplanting the testis to the opposite scrotal sac, using the scrotal raphé to prevent retraction; (5) fixating the

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From the Surgical Service of Dr. Milton Bodenheimer, Hospital for Joint Diseases.

1. (*a*) Bevan, A. D.: Operation for Undescended Testicle and Congenital Inguinal Hernia, J. A. M. A. **33**:773 (Sept. 23) 1899. (*b*) Goetsch, A.: Undescended Testis: Review of Thirty-Two Operative Cases, Am. J. Surg. **12**:63, 1931. (*c*) Love, A. G., and Davenport, C. B.: Defects Found in Drafted Men: Statistical Information Compiled from the Draft Records, Washington, D. C., Government Printing Office, 1920. (*d*) Marshall, H.: Contribution to Statistics of Hernia Among Recruits for the British and Conscripts for the French Army, Edinburgh M. & S. J. **50**:15, 1838. (*e*) Ziebert, K. A.: Ueber Kryptorchismus und seine Behandlung, Thesis, Heidelberg, 1898, Tübingen, H. Laupp, 1898.

2. (*a*) Burdick, C. G., and Coley, B. L.: Undescended Testicle, Ann. Surg. **84**:867, 1926. (*b*) Cabot, H., and Nesbit, R. M.: Undescended Testis, Arch. Surg. **22**:851 (May) 1931. (*c*) Guiteras, R.: Urology: The Diseases of the Urinary Tract in Men and Women, New York, D. Appleton and Company, 1912, vol. 2, p. 589. (*d*) Wangensteen, O. H.: The Undescended Testis, Arch. Surg. **14**:663 (March) 1927.

testis into the thigh; (6) multiple stage procedures, by which the testis is fixed temporarily to the posterior wall of the inguinal canal.

Orchidopexy for cryptorchidism was first reported by Rosenmerkel.[3] Bevan [1a] described a procedure in which the spermatic vessels are divided to allow the testis to enter the scrotum. Moschcowitz [4] used a similar procedure. Ombrédanne [5] brought the testis through the scrotal raphé so that both testes were in the same compartment of the scrotal sac. Cabot and Nesbit [2b] reviewed the various methods of placing traction on the testis and added the use of elastic traction to lengthen the cord and retain the testis in the scrotum. Multiple stage procedures for abdominal cryptorchidism have been described and successfully used by Cabot.[6] Keetley [7] and later Torek [8] suggested fixation of the testis into the thigh, and this procedure has been extensively used by several operators.[9] Burdick and Coley [10] have had the widest experience and achieved the most successful results with this method.

The importance of the endocrine biology of the testis was first brought into prominence by Sand [11] in 1918 by his experiments with cryptorchidism. The use of endocrine preparations in the treatment of undescended testes was instigated by the investigations of Zondek and Aschheim [12] and Evans and Simpson,[13] who demonstrated the gonadotropic principle in the anterior lobe of the pituitary gland. Moore [14]

3. Rosenmerkel, J. F.: Ueber die Radicalcur des in der Weiche liegenden Testikels bei nicht vollendetem Descensus desselben, Munich, K. Lindauer, 1820.

4. Moschcowitz, A. V.: The Anatomy and Treatment of Undescended Testis, with Especial Reference to the Bevan Operation, Ann. Surg. **52**:821, 1910.

5. Ombrédanne, L.: L'orchidopexie chez l'enfant, Gaz. méd. de France **2**:118, 1928.

6. Cabot, H.: Treatment of Abdominal Cryptorchidism, J. Mt. Sinai Hosp. **4**:596, 1938.

7. Keetley, C. B.: Temporary Fixation of Testis to Thigh: A Series of Twenty-Five Cases Operated on for Undescended Testis, Lancet **2**:279, 1905.

8. Torek, F.: The Technique of Orchidopexy, New York M. J. **90**:948, 1909.

9. Meyer, H. W.: Undescended Testicle, Surg., Gynec. & Obst. **44**:53, 1927. Wangensteen, O. H.: The Surgery of the Undescended Testis, ibid. **54**:219, 1932. Cabot.[6]

10. Burdick, C. G., and Coley, B. L.: Undescended Testicle, Ann. Surg. **98**: 495, 1933.

11. Sand, cited by Møller-Christensen, E.: Ueber Kryptorchismus und seine Behandlung mit Sexualhormonen, Acta path. et microbiol. Scandinav., 1938, supp. 37, p. 391.

12. Zondek, B., and Aschheim, S.: Hypophysenvorderlappen und Ovarium: Beziehungen der endokrinen Drüsen zur Ovarialfunktion, Arch. f. Gynäk. **130**:1, 1927.

13. Evans, H. M., and Simpson, M. E.: Antagonism of Growth and Sex Hormones of the Anterior Hypophysis, J. A. M. A. **91**:1337 (Nov. 3) 1928.

14. Moore, C. R., and Price, D.: Some Effects of Fresh Pituitary Homoimplants and of the Gonad-Stimulating Substance from Human Pregnancy Urine on the Reproductive Tract of the Male Rat, Am. J. Physiol. **99**:197, 1931.

showed the action of chorionic gonadotropin on the reproductive tract of the male rat. Cole and Hart [15] found a gonad-stimulating substance in the serum of pregnant mares which was effective in increasing the size of the testes of the rat, and Engle [16] found that extracts of the anterior lobe of the pituitary gland were effective in causing descent of the testes in the prepubescent monkey.

Browne,[17] along with several other investigators,[18] expressed the opinion that endocrinotherapy for this condition is useless and even dangerous and warned of harmful results. Eisenstaedt,[18c] in noting the degenerative and injurious effects of endocrine preparations on the undescended testis, expressed his belief that such treatment makes subsequent operative intervention more difficult. One result of his investigations which is of great importance is that comparatively enormous doses of chorionic gonadotropin administered to animals did not cause any ill effects in those animals in which the testis was in the normal position. In a recent article, Johnson [19] expressed the belief that endocrinotherapy should be used only as adjunctive therapy in cases of oncoming puberty. From a careful review of 15 cases of cryptorchidism treated with chorionic gonadotropin (I personally followed many of the patients over a period of one year), Arnheim [20] concluded that failures with chorionic gonadotropin (follutein) are most often due to mechanical obstructions which require surgical intervention and that even in these cases such therapy is valuable.

Goldman [21] used large doses of chorionic gonadotropin in a carefully studied group of 11 cases and had successful results in 10 cases. In a

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15. Cole, H. H., and Hart, G. H.: The Potency of Blood Serum of Mares in Progressive Stages of Pregnancy in Effecting the Sexual Maturity of the Immature Rat, Am. J. Physiol. **93**:57, 1930.

16. Engle, E. T.: The Action of Extracts of Anterior Pituitary and of Pregnancy Urine on the Testes of Immature Rats and Monkeys, Endocrinology **16**:506, 1932.

17. Browne, D.: The Diagnosis of Undescended Testicle, Brit. M. J. **2**:168, 1938.

18. (*a*) Cabot, H.: Management of Patients with Retained Testes, Radiol. Rev. & Mississippi Valley M. J. **58**:198, 1936. (*b*) Cole, H. H.: On the Biological Properties of Mare Gonadotropic Hormone, Am. J. Anat. **59**:299, 1936. (*c*) Eisenstaedt, J. S.; Appel, M., and Fraenkel, M.: The Effect of Hormones on the Undescended Testis, J. A. M. A. **115**:200 (July 20) 1940. (*d*) Mimpriss, T. W.: The Treatment of Imperfect Descent of the Testes with Gonadotropic Hormones, Lancet **1**:497, 1937.

19. Johnson, W. W.: Cryptorchidism, J. A. M. A. **113**:25 (July 1) 1939.

20. Arnheim, R. E.: The Treatment of Undescended Testes with Gonadotropic Hormones, J. Mt. Sinai Hosp. **4**:1036, 1938.

21. Goldman, A.; Stern, A., and Lapin, J.: The Treatment of Undescended Testes by the Anterior Pituitary-Like Principle from the Urine of Pregnancy, New York State J. Med. **36**:15, 1936.

review of 117 cases of cryptorchidism, Fèvre and Eck [22] stated that they used chorionic gonadotropin and testosterone propionate successfully in the treatment of this condition. They expressed their opinion that up to puberty endocrinotherapy should be used and that then, if necessary, operation should be performed. They used the transscrotal procedures suggested by Ombrédanne.[5] In an extensive review of the problem of undescended testis, Thompson and Heckel [23] commented that it is important to maintain an open mind about endocrinotherapy, although they stated their belief that many of the reports have been overenthusiastic.

It is not my purpose, nor is it within the scope of this report, to review the entire results of endocrinotherapy on the descent of the testis or to enter into the controversy on this subject. Suffice it to say that since the aforementioned experimental scientific contributions were made, many investigators and clinicians have attempted to influence the course of cryptorchidism by the use of several endocrine preparations with varied and controverted results.[24]

With varying degrees of success, several different endocrine preparations have been used in an attempt to effect the descent of the testis to the normal position. Those credited with the greatest success are: thyroid, gonadotropic substance recovered from the urine of pregnant women, gonadotropic substance recovered from placental tissue, gonadotropic substance recovered from the serum of pregnant mares, desiccated pituitary gland substance (given orally), extracts of the anterior lobe of the pituitary gland and testosterone proprionate. Various combinations of these preparations have been used. It is probable that more adequate methods of purifying extracts and further study concerning the chemical nature and synthesis of these and other endocrine preparations will make their use in properly selected cases more successful.

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22. Fèvre, M., and Eck, R.: Etude clinique et thérapeutique de l'ectopie testiculaire, Ann. méd.-chir. **3**:339, 1938.

23. Thompson, W. O., and Heckel, N. J.: Undescended Testes, J. A. M. A. **112**:397 (Feb. 4) 1939.

24. Aberle, S. B. D., and Jenkins, R. H.: Undescended Testes in Man and Rhesus Monkeys, J. A. M. A. **103**:314 (Aug. 4) 1934. Cohn, S.: Anterior Pituitary-Like Principle in the Treatment of Maldescent of the Testicle, ibid. **103**: 103 (July 14) 1934. Dorff, G. B.: Maldevelopment and Maldescent of the Testes, Am. J. Dis. Child. **50**:1429 (Dec.) 1935. Drake, C. B.: Spontaneous Late Descent of the Testis, J. A. M. A. **102**:759 (March 10) 1934. McCahey, J. F.: Gonadotropic Hormone Therapy in Cryptorchidism and Disturbances of Spermatogenesis, Pennsylvania M. J. **41**:359, 1938. Rea, C. E.: Further Report on Treatment of Undescended Testes by Hormonal Therapy at the University of Minnesota Hospitals: Discussion of Spontaneous Descent of Testis and Evaluation of Endocrine Therapy in Cryptorchidism, Surgery **7**:828, 1940. Schapiro, B.: Kann man mit Hypophysenvorderlappen den unterentwickleten männlichen Genitalapparat beim Menschen zum Wachstum anregen? Deutsche med. Wchnschr. **56**:1605, 1930. Eisenstaedt, Appel and Fraenkel.[18c]

It would seem that testes which have failed to descend because of an endocrine imbalance either before birth or in the early years of life might be brought into normal position by adequate physiologic (endocrine) stimulation. The descent of testes which are abnormally located because of anatomic failure and pathologic change will not be affected by endocrinotherapy, and surgical intervention becomes an obvious necessity.

It is possible that the discrepancies in the results of reliable observers are due to: (1) variability in the type, the potency and the dosage of the preparations used; (2) lack of anatomic classification between undescended, maldescended and ectopic testes; (3) lack of selectivity of patients for the type of treatment instituted—that is, physiologic (endocrine) treatment has been given to patients requiring early surgical intervention, and operation has been performed on patients who might have been amenable to physiologic (endocrine) therapy. It is important in deciding the treatment to be used in each case to determine whether various endocrine stigmas, such as infantilism, eunuchoidism or other signs of endocrine abnormality, are present. Patients who appear normal in every respect with the exception of the testes can be considered less suitable for endocrinotherapy. Patients showing signs of underdevelopment due to endocrine insufficiency may show satisfactory progress when adequate doses of the proper preparation or preparations are administered.[25]

Engle [26] stated that in the descent of the testes following endocrinotherapy the subsequent increase in mass and weight are the most important factors. However, he qualified this by stating that the external inguinal ring must be open and the gubernaculum testis must be pulling downward. Browne [17] successfully classified and clarified those abnormal anatomic positions which the testis may assume and also attempted to point out the differentiation between the cases in which the testis will descend spontaneously and the cases in which surgical intervention is inevitable. His classification and observations may be of assistance as a guide to therapy. A more physiologic classification seems to be: (1) undescended testes, those which are found within the normal pathway of descent but for the malposition of which there is no anatomic explanation; (2) maldescended testes, those which are found within the normal course of descent but which are prevented from

25. Moricard, R., and Saulnier, F.: Développement artificiel de l'appareil génital par les esters de testostérone, Gynécologie **38**:272, 1939. Oberholtzer, A.: Ormoni testicolari sintetici; loro azione fisiologico ed impiego in terapia, con speciale riguardo alla cura della ipertofia prostatica, Arch. ital. di urol. **15**:181, 1938.

26. Engle, E. T.: Experimentally Induced Descent of the Testis in the Macacus Monkey by Hormones from the Anterior Pituitary and Pregnancy Urine, Endocrinology **16**:513, 1932.

entering the scrotum by some abnormality in the pathway, such as adhesions, anatomic abnormalities of the inguinal canal, malattachment of the gubernaculum and herniation; (3) ectopic testes, those which have entered the wrong planes of descent and are off their normal course, in the thigh, the os peroneum or the wall of the abdomen.

Despite the various controversial opinions in the literature on endocrinotherapy, a good deal of evidence has been accumulated to show the value of this type of treatment when properly administered; endocrinotherapy has effect not only on the growth and the development of the testis but on the entire genital apparatus, including the vas deferens, the epididymis and the scrotum.[27]

Reasons for operation in cases of cryptorchidism are as follows: (1) to introduce the testis into the scrotum (after puberty this is the only location in which the testis will produce both internal and external secretions normal in amount and character); (2) to prevent traumatic derangements of the testis (torsion, direct trauma), which occur much more frequently when the testis is in an abnormal position; (3) to anticipate and prevent malignant tumor of the testis, which occurs much more frequently when the testis is in an abnormal position (although there is still controversy concerning the frequency); (4) to obviate the psychic effects which this abnormality has on the growing boy and the adult man; (5) to serve as a part of the repair of inguinal herniation when present.

In my experience of over ten years on the surgical staffs of several institutions, I have had the opportunity to observe the results of both endocrine and operative treatment in a large number of cases of cryptorchidism.[28] It is my observation that neither type of treatment is completely successful in all cases. It is imperative to call attention to the fact that although it is an accomplishment to be able to show a palpable testis in the scrotum, it is equally, if not more, important to have this testis function normally.

An operative procedure which would retain the testis in its normal position (the aim from a surgical point of view) would also be advantageous in those selected cases in which postoperative physiologic (endocrine) therapy is indicated.

A method has been devised which I believe preferable when indicated, whether combined with endocrinotherapy or not. This operative technic is dependent on: (1) the retention of the testis in the scrotum

27. Robson, J. M., and Taylor, H.: Factors Influencing the Functional Development of the Male Gonad, Proc. Roy. Soc., London, s.B **113**:251, 1933. Smith, P. E., and Leonard, S. L.: Responses of the Reproductive System of Hypophysectomized and Normal Rats in Injections of Pregnancy-Urine Extracts, Anat. Rec. **58**:145, 1934. Engle.[26]

28. Burdick and Coley.[28] Moschcowitz.[4] Burdick and Coley.[10] Arnheim.[20]

by the use of a fascial flap reflected from the thigh; (2) the reattachment of a previously malattached gubernaculum; (3) the suturing of the scrotum to the thigh.

OPERATIVE TECHNIC

An inguinal incision is made adequate to expose both the internal ring and the neck of the scrotum (fig. 1 *A*). This must be varied according to the position of the testis.

Division of the fascia of the external oblique muscle down through the external ring is made, care being taken not to enter the hernial sac or injure the testis. The hernial sac is isolated and liberated from the structures of the spermatic cord. The gubernaculum is isolated and left attached, the sac being liberated and cut across near the internal ring and ligated. The distal segment of the sac is incised longitudinally and everted to envelop the cord and the testis and is then closed loosely with a running suture. Liberation of the adhesions between the vessels and the cord, especially of those adhesions about the internal ring, is now carefully carried out. By following the vessels directly upward retroperitoneally with blunt and sharp dissection and by separating all adhesions, the vessels are liberated to allow the use of their greatest length. Although the vas deferens usually has sufficient length, blunt dissection is carried out, retroperitoneally downward and medially, when necessary. After the liberation of the vessels and the vas deferens, their lengths are measured to ascertain the position of the testis in relation to the scrotum.

The scrotal sac is enlarged by manual dilation (a Goodell cervical dilator may be used) to make a bed for the testis, and an incision 1½ inches (3.8 cm.) long is made at its lateral inferior aspect. The gubernaculum testis is then grasped, and the testis is pulled down through the scrotal incision; the distance between the adjacent thigh and the testis is then measured (fig. 1 *B*).

At a site on the adjacent thigh within reach of and close to the scrotal incision an oblique incision 1½ inches (3.8 cm.) long is made from above downward and mesially, and the fascia lata of the thigh is exposed by retracting the lateral margin of this incision.

A fascial flap, 1 inch (2.5 cm.) wide, dependent in length on the distance of the testis from the thigh (anywhere from 1 to 3 inches [2.5 to 7.6 cm.]) is then cut from the lateral aspect of the exposed fascia and reflected medially toward the scrotum. It is important to cut and reflect this flap at such an angle that it points toward the testis in order that the flap will not be twisted at its base. If it is found that a long flap (2 or 3 inches [5 or 7.6 cm.]) will be necessary, ½ inch (1.3 cm.) incisions are made at each end of and at right angles to the incision in the thigh to facilitate exposure of the fascia.

When the fascial flap has been adjusted in length and direction to the position of the testis and the gubernaculum, the posterior lip of the scrotal incision is sutured to the medial lip of the incision in the

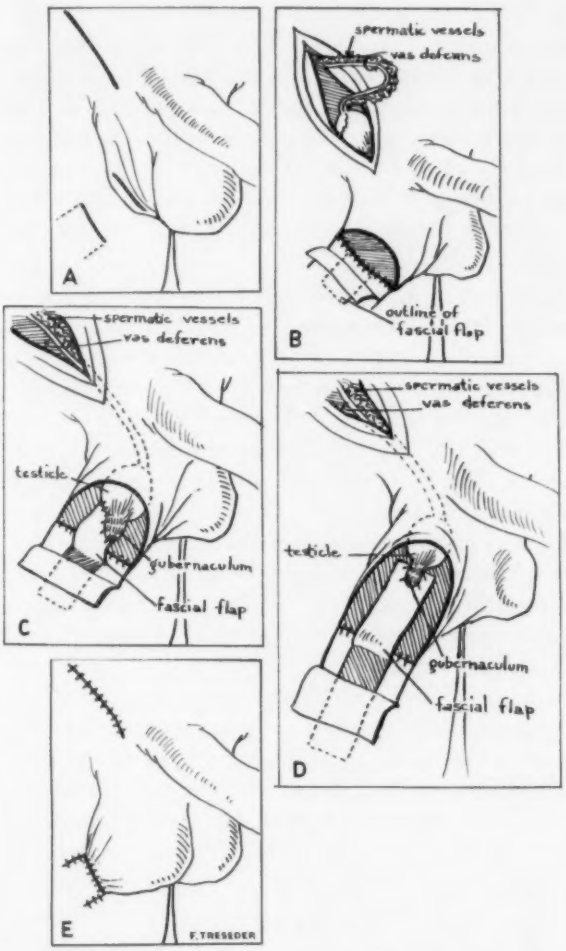

Fig. 1.—First stage of the operative treatment of cryptorchidism. *A*, location of incision; *B*, suture of the scrotum to the medial lip of the incision in the thigh and the outline of the fascial flap; *C*, attachment of the gubernaculum testis and the testicle to the fascial flap; *D*, attachment of the gubernaculum testis to the fascial flap alone; *E*, suture of the scrotum to the lateral lip of the incision in the thigh, thus completing the first stage.

thigh with interrupted sutures, great care being taken to approximate the edges of the skin accurately.

If the testis can be brought down to within 1½ inches (3.8 cm.) of the thigh, the fascial flap is reflected back toward the testis, and

two sutures are placed between the edge of the fascia and the tunica albuginea of the testis. The entire gubernaculum is then placed on the surface of the reflected fascia and attached by two or three carefully placed sutures (fig. 1 *C*).

If the testis cannot be brought down within 1½ inches (3.8 cm.) of the thigh without undue tension and the intervening distance is 1½ to 3 inches (3.8 to 7.6 cm.) the available gubernaculum alone is placed on the reflected surface of the fascia and sutured to it at whatever points they meet. No sutures are placed between the fascia and the tunica albuginea (fig. 1 *D*).

The anterior lip of the scrotal incision is now sutured to the lateral lip of the incision in the thigh; and if right angle incisions were necessary, they are closed with interrupted sutures. The scrotum now completely surrounds the anastomosis of the fascia to the gubernaculum and the fascial flap. The wound is dressed with petrolatum gauze (fig. 1 *E*).

Hernioplasty without transplantation of the cord is now effected by two or three mattress sutures (Ferguson method) to bring the conjoined tendon and the internal oblique muscle of the abdomen to the shelving edge of Poupart's ligament, and the external oblique muscle is closed with a running suture.

The second stage of this procedure is done any time from two to six months later. It consists in incising the skin and the fascial flap through the skin of the thigh leaving the scrotal skin intact and suturing the wounds. Care must be taken to trim and approximate carefully the edges of the scrotal incision.

The advantages of these procedures are as follows: (1) The spermatic cord is kept under constant tension; its length is thus increased, and retraction of the testis is prevented. (2) No foreign material is used for traction, and the fascia used is always available. (3) In cases in which it is not possible to lengthen the cord sufficiently to bring the testis into the thigh, the fascial flap is measured to bridge this gap. In cases of this sort this procedure can be used, even though the original intent was the Keetley-Torek operation. (4) The testis remains in the scrotum, its normal position, and is allowed to develop immediately on completion of the first stage (its sensitivity to temperature changes when out of the scrotum is well known). (5) The second stage is a simple procedure and does not endanger the testis. (6) If endocrinotherapy is indicated, it can be instituted immediately after the first stage, when the testis is in its normal position. (7) If the testis cannot be brought down to within 3 inches (7.6 cm.) of the thigh during the first stage (as it sometimes cannot be in cases of abdominal cryptorchidism), this can be done as a second stage after fixation of the testis to the posterior wall of the inguinal canal as suggested by Cabot.[6]

REPORT OF CASES

CASE 1.—V. C., admitted to the Hospital for Joint Diseases on Sept. 6, 1939, was a well developed white youth, 16 years of age, tall, slender and normal in contour. No endocrine stigmas were noted. Since childhood it had been known that only the left testis was present in the scrotum. The bulge which had been noted in the right inguinal region had grown larger in recent years, and the patient had been advised by the school physician to have his hernia repaired. The patient had no symptoms referable to the abnormal position of the testis. No therapy of any kind had been attempted for this condition.

Physical examination revealed one testis on the left side of the scrotum, about one and a half times the normal size. The scrotum was completely developed on this side. On the right side there was a right indirect inguinal hernia of the congenital type. The scrotal sac on this side was undeveloped and consisted of a slight redundancy of skin into which the hernia protruded. A small mass, the testis, was palpated at the internal ring, apparently having just entered the inguinal canal. It could not be moved further downward by manual effort but was easily reduced into the abdomen with reduction of the hernia. The remainder of the physical and laboratory examinations yielded entirely negative results, with the exception of hypertrophied tonsils.

Operation was performed three days after admission with the patient under general anesthesia. Incision in the right inguinal region revealed a large hernial sac which was easily dissected free of the surrounding tissues after incision of the fascia of the external oblique muscle down through the external inguinal ring.

On opening the hernial sac, the testis (about the size of a small olive) was found lying at the level of the internal ring. The vas deferens and the spermatic vessels, which were closely adherent to the hernial sac, were carefully dissected away, and the sac was divided in its proximal portion and ligated. The adhesions between the spermatic vessel and the vas deferens were separated and divided with blunt and sharp dissection, and both the vessels and the cord were liberated by blunt dissection retroperitoneally along their course. The distal portion of the hernial sac in which the testis lay was opened; the gubernaculum was isolated, and the redundant hernial sac was everted about the cord and the testis with a running suture. By manual dilation the right side of the scrotum was enlarged. It was found that the spermatic vessels and the vas deferens were now long enough to place the testis within the scrotum, although a moderate degree of tension was necessary. The scrotum was then incised, and the testis and the gubernaculum were brought out through the incision. An oblique 2 inch (5 cm.) incision was made in the adjacent thigh, and the fascia lata was exposed. A fascial flap 1 inch (2.5 cm.) wide and 2½ inches (6.3 cm.) long was reflected backward to the gubernaculum.

After the medial lip of the incision in the thigh had been sutured to the posterior lip of the scrotal incision, the gubernaculum was attached to the reflected fascial flap by several interrupted sutures without undue tension. The anterior lip of the scrotal incision was then sutured to the lateral lip of the incision in the thigh with interrupted sutures. The testis was felt in the fundus of the scrotum. The scrotal wound was dressed with petrolatum gauze, and the hernia was repaired by the Ferguson method with three mattress sutures (fig. 2).

After operation, the patient received daily injections for sixteen days of 200 rat units of chorionic gonadotropin. Both wounds healed rapidly. His postoperative course was complicated by a low grade febrile reaction due to tonsillitis; this

began on the twelfth postoperative day. The fever subsided after tonsillectomy. However, this incident and the added operative procedure prolonged his period of hospitalization until November 11.

Fig. 2.—Patient in case 1 after the first stage procedure.

Fig. 3.—Patient in case 1 after the completion of the second stage.

The patient returned to the hospital for a second stage procedure on Feb. 5, 1940. Operation was performed on February 7; it consisted of an incision through the scrotal skin flush with the thigh and an incision of the fascial flap. The wounds in both the thigh and the scrotum were sutured with interrupted sutures. The testis was observed to be approximately twice as large as it was previously and about two thirds the size of a normal testis. It was noted at this procedure that the flap connecting the testis to the thigh had greatly increased in thickness. A section of this tissue showed this increase to be due to hypertrophy of the muscular fibers of the gubernaculum.

Follow-up examination on September 15 revealed the testis to be about four fifths the size of a normal testis (although only two thirds as large as the opposite testicle) and to be freely movable in the scrotal sac (fig. 3).

CASE 2.—J. R., a 17 year old Negro youth, was admitted to the Hospital for Joint Diseases on Sept. 6, 1939, because of bilateral inguinal hernias and the absence of both testes from the scrotal sac. The patient suffered no inconvenience from these abnormalities. Several months prior to admission, he had received a series of injections of an endocrine preparation in an effort to cause descent of his testes, but no change was noted.

Examination revealed a well developed youth of normal size and contour. There were no endocrine stigmas. Both inguinal regions showed herniations of the congenital indirect type. The scrotum was underdeveloped. On the right side the testis was found in the inguinal canal about midway between the internal and the external rings. It could be moved farther downward by manipulation. On the left side the testis was palpated in the inguinal canal just at the internal

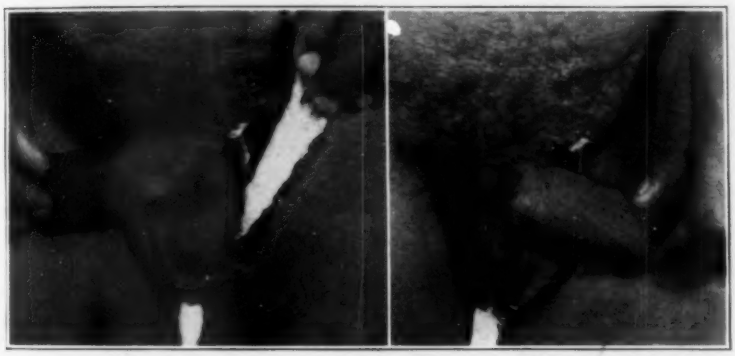

Fig. 4.—Patient in case 2 after the first stage procedure on the left side.

ring and could easily be reduced into the abdomen but could not be moved farther downward.

Operation on the left side was performed three days after admission, and a procedure similar to that performed in case 1 was carried out. The testis was observed to be about one half the normal size. The cord was lengthened by dissection. After separation from the hernial sac, the gubernaculum was isolated and found to be fairly large. The testis was brought down through an incision in the scrotum. Both the testis and the gubernaculum were anastomosed to the fascial flap reflected back from the thigh (fig. 4).

After operation there was a moderate amount of infection about the scrotal wound; this was successfully treated with wet dressings. The patient was given thirteen daily injections of 200 rat units each of chorionic gonadotropin and was discharged with wounds completely healed on October 12.

The patient was readmitted for the second stage procedure (already described in the report of case 1) on November 16. A section removed from the fascial flap attached to the gubernaculum showed thickening similar to that previously described. On this admission, it was noted that the testis on the side operated on was now enlarged to about 2.5 cm. in diameter, about two thirds the size of a normal testis, and that it hung freely within the scrotum. Seven injections of

Fig. 5.—Patient in case 2 after the second stage procedure on the left side.

Fig. 6.—Patient in case 2 after bilateral operative procedure; both testes are now in the scrotum.

200 rat units each of chorionic gonadotropin were administered following the second stage. The patient was discharged on November 28 (fig. 5).

The patient's third admission was on Feb. 9, 1940. At this time he was to have the hernia on the right side repaired and the right testis brought down. The left testis was now found to be normal in size and freely movable within the scrotum. The right testis had increased in size within the inguinal canal and had descended almost to the external ring. The operation was performed as previously described. A fascial flap, 1½ inches (3.8 cm.) long, was found sufficient and was anchored both to the testis and to the gubernaculum. The incisions in both the scrotum and the thigh healed rapidly, and the patient was discharged on March 1 after eleven daily injections of 200 rat units each of chorionic gonadotropin. The second stage procedure on the right side was performed on September 21 (fig. 6).

Both testes were observed to be normal in size and free in the scrotum. The patient was discharged on September 24.[29]

COMMENT

The possibility that abnormalities in the gubernaculum testis or its attachment are an actual or a predisposing cause to abnormal position of the testis has been considered likely by several authorities.[2]

In both cases reported the gubernaculum was malattached, in that it was densely adherent to the walls of the hernial sac and that the attachment was movable with the reduction of the hernia. Malattachment of the gubernaculum would nullify the effects of the force of the gubernaculum in causing normal descent of the testis. My experience along with that of others in several cases has shown that the further the descent of the testis from the normal position, the greater the persistence, at least in size, of the gubernaculum. In this operative procedure, therefore, the purpose of the attachment of the gubernaculum to the fascial flap is twofold: (1) to assist in retaining the testis in the correct position; (2) to correct the malattachment and give the gubernaculum a new attachment so that the pull is corrected and the force utilized to bring down and maintain the testis in the normal position.

It is of interest to note that from the sections taken from the union of the gubernaculum to the fascial flap in each case during the second

29. Since the completion of this article, the operation described has been performed on 2 patients at the United States Naval Hospital, Brooklyn. One patient was a man 45 years of age. The operation was done concomitantly with herniotomy. At the time of writing it is three months since these procedures were carried out; apparently both were completely successful. The second stage was done seven weeks after the original operations; by that time the testis was free in the lower pole of the scrotum. The second patient was 20 years of age. He had recurrent hernia following an unsuccessful attempt at orchidopexy ten years previously. In this procedure, despite the scarring and adhesions caused by the previous operation, it was possible to bring the testis down to the upper pole of the scrotum from the internal ring and to attach it with a moderate degree of tension to a fascial flap from the thigh. At the time of writing the testis is twice its former size (about one half as large as normal) and the second stage is to be performed in a few weeks.

stage procedure it is evident that the firm adherence of the gubernaculum to the fascia was due to an intermingling between the muscle bundles of the gubernaculum and the fascial fibers (figs. 7 and 8). This is added evidence in the controversy concerning the operative union of these two tissues.[30] It was also noted both clinically and microscopically that

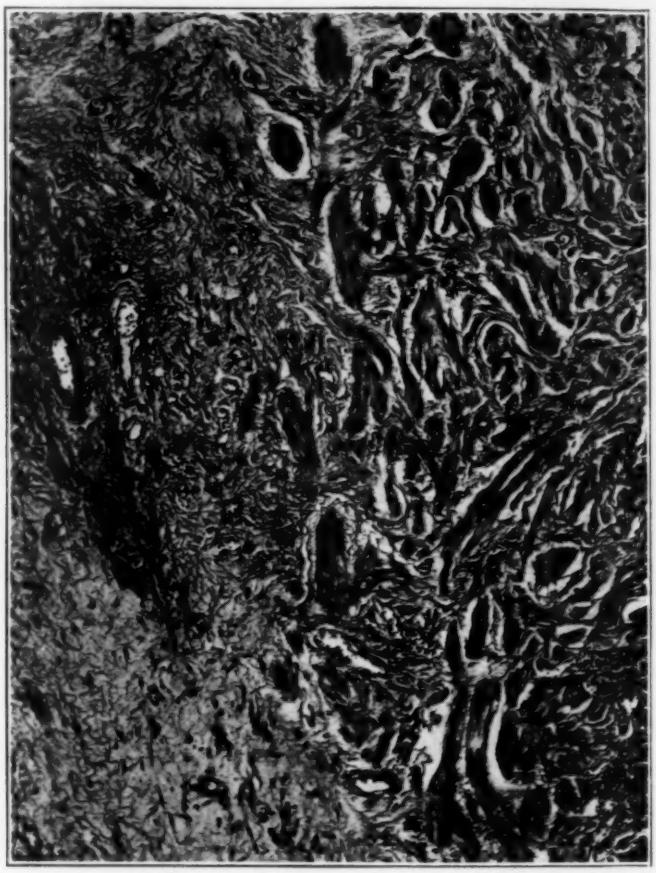

Fig. 7.—Photomicrograph of a section taken through the attachment of the gubernaculum testis to the fascial flap of the patient in case 1.

the muscular fibers of the gubernaculum had increased three or four times their original size. This thickening and increased tension of the gubernaculum followed endocrinotherapy, and it is possible that chorionic gonadotropin exerts an effect on the gubernaculum and indirectly on the

30. Haas, S. L.: The Union of Grafts of Live and of Preserved Fascia with Muscle: A Comparative Study, Arch. Surg. **23**:571 (Oct.) 1931.

descent of the testis. In an effort to prove this contention, experimental work with rabbits is now under way, and the result will be published on its completion.

It is worthy of note that both patients were comfortable between the first and second stages of this procedure and were hardly limited in their

Fig. 8.—Photomicrograph of a section taken through the attachment of the gubernaculum testis to the fascial flap of the patient in case 2.

activity. In fact, the patient in case 2 stated that between the first and the second stage on the right side he performed sexual intercourse normally. It is of importance also to report that examination of the semen of this patient after bilateral orchidopexy by the method described showed large numbers of highly mobile spermatozoa.

In the selection of suture material, there is a choice of chromic catgut, silk, linen or cotton. In case 2, silk was used on the right side

and linen on the left. Although clinical observation showed the side with linen to have less tissue reaction and a more mobile flexible scar, a section taken through the area containing the stitches showed that the linen caused a low grade foreign body reaction. In a more recent case, fine cotton proved entirely satisfactory. However, no matter which suture material is chosen, it is my experience that lightness and fineness are of more importance than the type of material used.

A word of warning should also be spoken concerning the use of gonadotropins. Although in competent hands with proper dosage of the correct substance good results may be accomplished in carefully selected cases, the many dangers involved in the use of these powerful agents must be realized. Often useless operative procrastination and permanent endocrine injury may result from lack of knowledge or from careless use of these preparations.[31]

Knowledge of the physiologic and chemical properties of endocrine preparations and their effects on specific tissues is increasing daily. Undoubtedly, when specifically potent and purified products are available and their effects on specific organs are known, the possibilities for intelligent endocrinotherapy will increase.

The surgical procedure which has been presented is suitable for use either with or without adjunctive endocrinotherapy, and I believe that physiologic stimulation should be used only when specifically indicated.

SUMMARY

The possible causes of failure of endocrinotherapy for cryptorchidism have been discussed.

A surgical procedure which can be combined with endocrinotherapy when indicated has been described, and the reports of 2 cases have been given.

The role of the gubernaculum testis in bringing about the descent of the testis, the susceptibility of the gubernaculum to endocrinotherapy and the possible use of this structure in a surgical procedure have been described.

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31. Collip, J. B.; Selye, H., and Thomson, D. L.: Histological Changes in the Hypophysis Produced by Chronic Administration of Hypophyseal Extracts, Proc. Soc. Exper. Biol. & Med. **31**:682, 1934. Eisenstaedt, Appel and Fraenkel.[18c]